

The Blastocyst and Placenta of the Beaver.

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With Plates 14 to 21 and 6 Text-figures.

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I. INTRODUCTION.

THE material upon which this contribution is based was collected by me during the seasons of 1911, 1912, and 1913. In the first season, at the Laurentides National Park in the

province of Quebec, the stage obtained between April 18th and April 27th was that of the submature naked foetus. In the second season, at the Algonquin Park in the province of Ontario, from May 1st to May 14th, the mature fur-covered foetus was procured. In the third season, from February 21st to March 11th, in the Lake Edward district between Quebec and Lake St. John, the stages of the early blastocyst and the young placenta were acquired. The result of my first visit to the woods of eastern Canada was published in the second volume of Prof. Spengel's 'Festschrift' (1912). In that paper there will be found the description of a strong extra-placental or periplacental connecting membrane, the "umbilico-uterine ligament," by which the large foetal sac is suspended from the wall of the gestation sac. This was one of the points that stood in need of further elucidation from new material.

In February, 1913, through the good offices of Profs. J. G. Adami and P. E. Nobbs, of this University, an opportunity for making an effort to secure earlier stages in the development of the beaver was presented to me. To Prof. Adami I am indebted for his kindness in apprising me of the fortunate occasion; while Prof. Nobbs, in the most generous manner, gave me the temporary freedom of a game reservation in which he was interested, together with the use of a hunting-lodge, compactly built of rough-hewn logs, situated on the shore of Lac Gagnon, near Pearl Lake, which is a few miles south of Lake Edward, on the line between the city of Quebec and Lake St. John. I spent eighteen days on this reservation, accompanied by a French Canadian gardien, skilled in woodcraft, named David Fournier, and a French Indian tracker named Joe Moreau. The severity of the season may be judged from the fact that the temperature ranged from -35° Fahr. (February 25th, at 6.30 a.m.) to $+26^{\circ}$ Fahr. (March 10th, at 1 p.m.).

We succeeded in getting some very young gestation sacs, which were preserved in 10 per cent. formalin. In the summer I brought this material to Europe, and, being

desirous of working upon it without undue delay, I wrote to Prof. Hubrecht, who promptly assured me of a welcome at Utrecht, so that I was able to enjoy the privilege of continuing the research in the Embryological Laboratory of the University of Utrecht for nine weeks, from May 30th to July 31st inclusive. I am deeply grateful to Prof. Hubrecht for his friendship, for the use of his laboratory with all its excellent facilities, for access to the library and to his collection of reprints, and particularly for his criticism upon various questions raised by the preparations, which at the beginning presented puzzling and unique appearances.

The material having been transferred from formalin to alcohol, the several gestation sacs were stained in toto with hæmalauun, serial sections cut, mounted, and counter-stained by Mr. J. G. de Groot, Conservator in the Embryological Laboratory at Utrecht. The preparations have been deposited in the collection of the Institut International d'Embryologie, which was established at Utrecht by Prof. Hubrecht in 1911. Most of the drawings illustrating this paper were made with the assistance of Edinger's "Zeichenapparat." Some of the more finished drawings have been executed by Mr. John Prijs, artist at the Institute, with the kind permission of Prof. Hubrecht.

In addition to the two youngest broods, which were the principal fruit of my third journey, and the only material collected before I left the reservation, later stages were forthcoming by arrangement with the gardien, who forwarded two subsequent consignments to me after my return to Montreal. These included the stage of the half-grown placenta and that of the two-thirds-grown placenta. I made drawings of the more advanced stages in Montreal, but the study of the youngest stages was carried out, as mentioned, in Utrecht.

Finally, I must not omit to acknowledge the assistance in procuring material from the Algonquin Park in 1912, with which I was favoured by Mr. G. W. Bartlett, the Super-

intendent, and by the park rangers stationed at Joe Lake, Messrs. James Bartlett and Mark Robinson.

II. SEX OF THE FŒTUS.

Before entering upon the description of the early stages, reference may be made to the question of the sex of the advanced fœtus. In 1911, of two beavers with young, one contained four fœtuses in the right uterus, the other carried two in the right uterus. There was none in the left horn of the uterus in either case, and all six fœtuses happened to be males. In 1912 I was informed that one gravid beaver had been caught, skinned, and buried several days before my arrival at Joe Lake. When we exhumed the carcass it was evident that the cool sandy loam had kept it perfectly fresh. It yielded five fœtuses, the only fœtal material obtained during the trip. There were three fœtuses in the right horn of the uterus, and these were all males. Of the two remaining fœtuses in the left horn, the one near the oviducal end was a female, the other near the cervical end of the uterus was a male. The male sex of the three right fœtuses thus happens to be consistent with the previous observations, but I am not disposed to lay undue stress upon the coincidence. Still it is well to put such data on record in the presumption that in future years some other observer may similarly rescue trapped beavers from their sandy sepulchre and determine the sex of the unborn young. Out of a total of eleven fœtal beavers whose sex has been determined, ten were males, nine of which were lodged in the right uterus, which has not yielded a female according to present information.

It seems doubtful whether the determination of fœtal sex in a large number of cases would justify the time and expense which would have to be devoted to it. Such data can only be accumulated by recording casual observations of no immediate value in themselves, but likely to be useful for future comparisons. Perhaps it is because occasional determinations seem to be so trivial that there is such a

paucity of references to the curious distribution of the sexes. The records would possibly have an additional interest if the age of the parents could be ascertained, but this is practically impossible in the case of the beaver. The isolated position of the beaver amongst rodents perhaps renders it worthy of special consideration in regard to this matter of the sex of the foetus which are lodged in the right and left horns of the uterus respectively. As for the apparent preponderance of males, it is known how misleading even impressive numbers may be in regard to the proportions of the sexes of various animals. Thus, in 1911, six females were captured and six foetal males extracted from two of them. In 1912 beavers were being taken alive in muffled traps and the sex was not always ascertained. My notes contain records of seven females and ten males, including male and female "kittens," two-year-olds and adults. These small numbers, so far as they go, would indicate an approximate equality of the sexes.

With regard to the remarkable multiple embryos of Armadillos, **M. Fernandez** (1909), investigating the case of the "Mulita" (*Tatusia hybrida*), where the embryos are in packets of about eight (varying in number from seven to twelve) contained within a common chorion and derived from a single ovum, noted that out of nine sets, three were all males, six all females; but as the material belonged to different regions and years it remained doubtful whether the excess of females had any significance. **Newman and Patterson** (1909, 1910), working independently about the same time upon the nine-banded Armadillo (*Tatusia novemcincta*), where the embryos occur as quadruplets, found that out of thirty-eight embryonic vesicles exactly half were male and half female. "All embryos in a vesicle are of the same sex," as was originally recorded for the "Mulita" by **H. von Jhering** in 1885, and only one set is produced at a time.

Newman and Patterson (1910) state that it has been known to the natives of Paraguay and of Argentina for over a century that the "Mulita" brings forth at a birth a litter of

young all of one sex. The nine-banded Armadillo does the same; and for this species **Newman** and **Patterson** have found that "there is no correlation between the sex of the embryos and the dextrality or sinistrality of the functional ovary. Out of twenty cases in which the right ovary contained the corpus luteum, the sex of the embryos was male in seven and female in thirteen; while out of thirteen cases in which the left ovary held the corpus luteum, the sex was male eight times and female five. Evidently, then, the position of the functional ovary has no determining influence on sex."

I will conclude this chapter with a couple of miscellaneous notes relating to the beaver. On May 2nd, 1912, a large pregnant female was caught alive by the toes in a muffled trap. On the following day she was taken in a sack to headquarters at Algonquin Park, and on May 10th gave birth to two kittens about 9 a.m.; at 10.30 a.m. it was noticed that their eyes were open. Towards the end of the day two more were born. The successful rearing of the kittens was ardently hoped for, but was frustrated by their death within two or three days. On May 14th a large male was trapped, measuring 42 in. from tip to tip. It had lost both of its fore-limbs at two previous trappings. The scars of the amputated members had healed up completely. This serious maiming would prevent the beaver from doing its share of work at the lodge and dam, but would not destroy its swimming and feeding powers. It need scarcely be stated that the traps which are set for beaver are concealed as far as possible, and much care is devoted to placing them in the most likely position from the trapper's point of view, so that it says nothing for or against the intelligence of the beaver that after two sad experiences the third proved fatal.

III. THE PREPLACENTAL BLASTOCYST.

The most conspicuous feature of the preplacental blastocyst of the beaver is the presence of a deep keel along the length of its embryonic side.

The Rodentia, as was first made known by the pioneer researches of **Bischoff**, show a great diversity in the ontogeny of the foetal sac, though the end-result is fairly uniform, and the discoplacenta is always mesometric in position. The divergent behaviour of the early blastocyst within the limits of the order involves different methods of amniogenesis. "Schizamnion" is the term used by **R. Bonnet** for the amnion which arises by dehiscence in a solid embryonic knob. He contrasts it with the more familiar "Faltenamnion," which I will translate into pleuramnion.

Whereas *Mus* and *Cavia* possess an inverted blastocyst and a schizamnion, *Lepus* and *Sciurus* have a plano-convex blastocyst and a pleuramnion; and it may be said that *Castor* has an everted blastocyst and pleuramnion, in the sense that the embryonic area and adjacent parts project as a sharp-edged keel which floats in the mesometric cavum. The shape of the blastocyst conforms to that of the cavity of the gestation sac or cavum uteri. Reference to Pl. 14, fig. 1, will make this point clear. Here we see the highly characteristic appearance of the walls and cavity of one of the uterine swellings containing a blastocyst in transverse section. There is a round wide portion occupying the antimesometric division and a narrow deep portion in the mesometric division of the gestation sac: the former is the omphaloid cavum, the latter the mesometric or placental cavum.

Lodged securely in the omphaloid cavum is the balloon-shaped omphalon, and projecting freely into the placental cavum is the keel. The longitudinal diameter of the blastocyst is greater than its transverse diameter. Omphalon is a convenient term introduced by **A. J. Resink** (1904) in place of "Dottersack" or "yolk-sac," as applied to the blastocyst of placental mammals.

The keeled blastocyst is attached to the obplacental wall of the omphaloid cavum by means of trophoblastic implantations which substitute themselves in places for the uterine epithelium. There is no constant symmetry in the distribution of the areas of fixation, but a certain degree of regularity may

be detected. Sometimes a single trophoblast cell will take the place of a uterine epithelial cell as shown in Pl. 14, fig. 2, where the implantation takes the form of a festoon-like arrangement. In other places the substitution is more extensive, as in Pl. 14, fig. 3; and sometimes there is a broad arc of adhesion involving the greater part of the dome of the blastocyst, but sparing the mouths of the glands, as is shown in Pl. 14, fig. 4.

The cells which constitute the obplacental trophoblast, surrounding the dome of the blastocyst, are megalokaryocytes¹ (large cells with large nuclei) of two intergrading kinds. This trophoblast, as we shall see hereafter, is engaged in the ingestion and absorption of three visible maternal products: (1) The albuminous fluid secreted by the uterine glands, which appears as a dense coagulum in the *cavum uteri*; (2) darkly staining granules, which are the lobed nuclei of leucocytes; (3) red blood-corpuscles.

The cells which ingest the leucocytes with their characteristic lobular nuclei may be named chromatophile megalokaryocytes, or more simply, chromatophile trophoblast. This is usually quite free from the uterine wall, the coagulum intervening; and at these places the uterine epithelium remains intact or but slightly altered. The normal megalokaryocytes which ingest maternal erythrocytes are those which attack the uterine epithelium and take its place upon the surface of the mucosa. In the placental or carinal hemisphere of the blastocyst, the megalokaryocytes pass quite gradually into the cubical ectoderm of the keel.

As stated above, there is some regularity in the disposition of the different kinds of trophoblast, and this necessitates the employment of descriptive topographical terms. The semi-diagrammatic fig. 5 on Pl. 14 shows the completest differentiation of regions of the trophoblast and of the mucosa with which it is associated. At the summit of the dome there is an area of trophoblastic implantation marking out the coronal region. On either side of this we have a tract

¹ J. W. Jenkinson (1902).

of free chromatophile trophoblast occupying the pericoronal region of the blastocyst; between this and the uterine epithelium, here intact, there is a narrow pericoronal cavity into which glands open. Beyond the well-marked pericoronal tract there follows a zone which can sometimes be differentiated into two portions: the part next to the pericoronal tract may be distinguished as the equatorial or periomphaloid tract, and the subequatorial festooned implantation may be known, by scientific license, as the pericarinal tract. Between the latter and the keel there extends a nearly horizontal omphalopleuric membrane of very constant formation, the adcarinal membrane. Lastly follows the keel or carinal region, which includes the embryonic shield and extra-embryonic keel.

The gestation sacs which contained preplacental blastocysts were six in number, and were extracted from one female on March 10th, 1913, three in each horn of the uterus. The swellings varied slightly in size, and the differences proved subsequently to be connected with the state of development. The average diameter of the swellings was 10 mm. The lowest swelling in the left horn measured 11 mm., the middle and upper about 10 mm. The lowest right swelling measured 10 mm., the middle right 10 mm., the upper right (i. e. nearest the Fallopian tube) 8 mm.

On March 4th I had obtained two gestation sacs 25 mm. in diameter, and on March 10th four more of similar dimensions. These dates seem to indicate that the typical stage at this part of the season is that of the young established placenta, but that the reproduction of the beaver does not take place with absolute precision between fixed dates, although the pairing season is known to be relatively constant. To the range of fluctuation that exists I owe the fortunate acquisition of the preplacental blastocysts. No two of these blastocysts are exactly alike, the six individuals representing as many substages which exhibit the characteristics of three main phases in the growth of the tridermic blastocyst: (*a*) with solid mesoblast; (*b*) with exocœlom; (*c*) with incipient

notochord. I will now proceed to the more detailed description of the successive substages of the preplacental blastocyst. Three of them are well-defined, the other three are more transitional.

IV. SUBSTAGE A.

This stage is represented by a series of sections, cut from before backwards relatively to the embryo, transverse to the longitudinal axis of the uterus, numbered VI B in the Utrecht catalogue. It is a critical stage, inasmuch as it affords the key to the comprehension of subsequent stages. The primitive streak occupies nearly the entire axis of the blastodisc, the mesoblast is solid throughout, and there is no notochordal contact between endoderm and medullary plate. It is the smallest of the swellings, having the following sectional dimensions:

	Millimetres.
Total height of gestation sac or uterine swelling, from root of mesometrium	8·50
Total diameter of gestation sac	5·50
Total height of <i>cavum uteri</i> or cavity of gestation sac	4·50
Depth of mesometric groove or placental <i>cavum</i>	3·00
Diameter of ditto	0·25 to 0·50
„ <i>omphaloid cavum</i>	1·00
Thickness of placental mucosa, between root of mesometrium and bottom of placental groove	3·00
Thickness of placental trophospongia or maternal proliferation	1·25
Thickness of periplacental wall or lateral wall of <i>cavum uteri</i> at each side of the placental groove	2·75
Thickness of obplacental wall of gestation sac	1·50

The thickness of the placental mucosa is given in the above table in order to exhibit its contrast with that of the obplacental wall; it includes the layer of circular muscles which

passes across the placental wall of the gestation sac between the root of the mesometrium (in which the main trunks of the uterine vessels occur) and the placental trophospongia. These transverse fibres of the circular muscles in the placental region become interrupted and oblique to a varying extent in later stages. The diameter of the omphaloid cavity is identical with that of the omphaloid portion of the blastocyst, or, in one word, the omphalon, because the trophoblastic wall of the omphalon is implanted upon the inner surface of the uterine mucosa, which becomes denuded of its epithelium at the points and areas of implantation.

The anterior pole of the blastocyst is free, and the embryonic area begins immediately behind the pole. The area itself is keel-shaped, since the embryonic shield of formative epiblast bends round the free edge of the keel. The formative epiblast which is thus exposed at the surface of the blastocyst is distinguished from the peripheral trophoblast by its nuclear constitution, by the fact that the nuclei occur at different levels, and also by the presence of scattered vesicular cells, i.e. embryonic cells in a vesicular phase. The transition from formative epiblast to peripheral trophoblast is singularly abrupt, there being no gradual transition from one to the other at the level where they meet.

The hypoblast dips into the keel, and, at a very short distance from the anterior end, we find in section the solid U-shaped tip of the mesoblast embracing the floor of the hypoblastic groove, with a few cells migrating out from it along the hypoblast (Pl. 14, fig. 6). The free end of the mesoblast has but slight longitudinal extension, since the primitive streak begins immediately behind it, so that we find in section a perfect U-shaped, solid mesoblast, united to the epiblast by the primitive streak. The position of the primitive streak marks the strictly embryonic side of the keel. The peripheral limits of the formative epiblast may be seen clearly under Zeiss oc. 2, obj. A; the edge of the shield is placed at a much higher level on the embryonic side of the keel than on the other side (Pl. 14, fig. 7).

From this point backwards the primitive streak is continuous, and presents various incidents of growth at different parts of its length. The wedge-like proliferation at Pl. 14, fig. 8, followed by the chink-like cleft in Pl. 14, fig. 9, lies near the anterior end. From the V-shaped mass which proceeds from the primitive streak and embraces the hypoblastic groove a single line of mesoblast cells extends on each side along the hypoblast, about as far as the equatorial region of the blastocyst at this early stage. Later, the mesoblast has a much more restricted peripheral distribution. The juxtaposed walls of the epiblastic keel distad of the primitive streak become closely welded together.

The lateral wings of the mesoblast are in close contact with the hypoblast, but are separated from the epiblast except at the primitive streak. This is especially obvious on the anti-embryonic side of the keel (Pl. 14, fig. 10). The embryonic shield becomes narrower as it is traced backwards, so that its peripheral limits are much lower than in front; on the anti-embryonic side the edge of the formative epiblast reaches the level of the welded walls of the keel, and finally the apex. A small pit appears intermittently at the surface of the primitive streak, but there is no continuous primitive groove (Pl. 14, fig. 11). The mesoblastic wings become unequal as we near the posterior end of the primitive streak, that on the embryonic side being longer than the part which bends round to the anti-embryonic side (Pl. 14, figs. 12 and 13). In this situation it is easy to recognise that the anti-embryonic wall of the keel consists of cubical trophoblast, the embryonic wall of formative epiblast. The keel is thus partly embryonic and partly extra-embryonic in the same transverse section.

Posteriorly the primitive streak contact widens and the distal border of the keel consists of cubical trophoblast only (Pl. 14, fig. 14). In this region we see very clearly a broad primitive streak with mitoses, and no other formative epiblast. One limb of the mesoblast becomes very slender, the other limb dwindles to zero, whilst the bulk becomes massed about

the primitive streak, partly blocking up the cavity of the trophoblastic keel. Shortly behind this region the primitive streak ceases and the mesoblast rapidly diminishes until only a single line of cells remains on one side of the hypoblast as in Pl. 14, fig. 15.

Finally, the mesoblast terminates and the keel becomes didermic. At the same time the two layers are badly folded in the sections owing to a collapse which apparently resulted from rupture of the adcarinal membrane. This fact, added to the great local differences in the character of the epithelial walls of the blastocyst, seems to point to the existence of a considerable amount of elasticity in the inner and outer membranes. In this case the rupture seems to have been due to an extraordinary agglutination of the adcarinal trophoblast on one side to the edge of the placental groove. This adhesion was retained whilst the rest of the blastocyst followed the contraction of the coagulum contained within the omphalon; except for this unusual attachment, the blastocyst would be free at this level. A little farther back the hypoblast withdraws, leaving a trophoblastic keel with its walls welded together distally. Thus we have a trophoblastic keel near the posterior pole of this blastocyst, but not near the anterior pole where the keel is embryonic. The keel formation gradually dwindles away as the posterior pole is reached.

I will postpone the history of the uterine mucosa until the other substages have been dealt with, but a few words are necessary concerning the fixation of the blastocyst. The anterior pole which lies in front of the primitive streak projects freely into the *cavum uteri*; the posterior pole is fixed with a broad obplacental implantation. Between the free anterior pole and the middle of the blastocyst there is a region corresponding approximately with the middle of the primitive streak where obplacental arcades become established, i. e. intermittent areas of trophoblastic implantation with destruction of uterine epithelium at the points of contact. About the level of the posterior end of the primitive streak, which is about the middle of the blastocyst, the obplacental contact

is given up except at the two pericoronal corners, where a very narrow implantation is retained as in Pl. 14, fig. 13. Between these two angles there extends the free coronal trophoblast, whose cells contain chromatic granules identical with those which occur in the intervening coronal cavum and in the mucosa. I have determined them to be the nuclei of leucocytes. The leucocytes migrate across the uterine epithelium into the cavum uteri and are ingested by the chromatophile megalokaryocytes.

Towards the posterior pole of the blastocyst the active phagocytic attack is resumed, the megalokaryocytes broadly replacing the uterine epithelium, with formation of arcades, skipping the crypt-like mouths of the obplacental glands. In the coronal region there is no visible sign of hypoblast which appears to stop short about the equatorial zone of the blastocyst. The hypoblast comes to an end posteriorly coincidentally with the termination of the trophoblastic keel, so that the extreme posterior pole of the blastocyst is monodermic, its wall consisting entirely of flattened cells with distant nuclei, appearing subfusiform in section.

At no stage is the hypoblast conspicuous in the coronal region, but sometimes straggling cells can be found.

V. SUBSTAGE B.

This is represented by a series of transverse sections cut from before backwards and numbered VI D in the Utrecht Catalogue. It is characterised by the first indication of a linear exocoelom.

	Millimetres.
Height of gestation sac	10·00
Diameter of gestation sac	7·75
Height of cavum uteri	6·00
Depth of placental groove	4·00
Diameter of placental groove near bottom .	0·30
" " " about the centre	0·90
" " " omphaloid cavum	2·00

	Millimetres.
Thickness of placental mucosa	3·00
„ placental trophospongia . about	1·75
„ periplacental wall	3·50
„ obplacental wall	1·10

These measurements, especially as regards the diameter of the omphaloid cavum, show that this substage is intermediate between that described above and that which follows below. The blastocyst covers thirteen slides, with twenty-four sections, 10 μ thick, on each slide; hence the length of the preserved blastocyst is 3·12 mm., its transverse diameter being that of the omphaloid cavum, viz. two millimetres. In front of the blastocyst the omphaloid cavum contains a homogeneous coagulum which has shrunk away from the epithelium upon which it was moulded; in it are scattered cellular débris and chromatic (leucocytic) granules.

The anterior pole of the blastocyst is free; the trophoblast here consists exclusively of megalokaryocytes, and a few hypoblast cells appear against its mesometric wall, not forming a closed hypoblastic sac. The megalokaryocytes exhibit coarsely alveolar cytoplasm and contain a few chromatic granules. The blastocyst appears in section quite free in the centre of the uterine coagulum; its own internal coagulum is reticulated and paler than the surrounding coagulum. Near to the anterior pole the blastocyst is pyriform in section, the narrow portion only being didermic (Pl. 15, fig. 16). Farther back, the blastocyst still appearing free in section, a long keel arises, somewhat folded in the preparation, composed of cubical trophoblast. The hypoblast is now seen to pass uninterruptedly over the cavity of the keel (Pl. 15, fig. 17). About this same region, where the free anterior end of the blastocyst possesses the long trophoblastic keel, as many as nine glandular crypts were counted, opening into the omphaloid cavum.

The plane of the blastocyst represented in fig. 17 shows well the two kinds of trophoblast composing the outer wall, namely, the omphaloid trophoblast with its megalokaryocytes

karyocytes, and the carinal trophoblast with its cubical cells. Shortly behind this plane the omphaloid trophoblast begins to attack the uterine epithelium at intervals. Here and there the direct passage of leucocytes with their lobed chromatic nuclei may be exceptionally observed to take place from the mucosa into the coronal trophoblast. As we proceed backwards we come upon conspicuous obplacental attacks by megalokaryocytes between the mouths of the glands, and a broad pericarinal attack on one side only. The pericarinal zone is doubled by hypoblast which does not cover the obplacental half of the omphalon in this plane. The pericarinal adhesion is characterised by the formation of festoons; at the periomphaloid zone, just beyond the pericarinal festoons, there has taken place an ingestion of erythrocytes by the trophoblast. This also occurs in the coronal region, where there arises a broad adhesion bounded on each side by a free belt of pericoronal chromatophile trophoblast with the megalokaryocytes full of granules. The attacking trophoblast abuts, in a manner which is as clear as it is surprising, upon the columnar epithelium of the glandular orifice, two or three trophoblast cells bridging over the gaps as shown in Pl. 14, fig. 4.

Upon approaching the embryonic region we find, in this series, a confused mass of hypoblast and mesoblast collapsed at the foot of the keel, almost defying interpretation, until we come to the region of the primitive streak. There we see an extension of the process which commenced in the preceding stage, namely, the filling up of the keel by a mass of mesoblast derived from the primitive streak. Into this massive carinal mesoblast the hypoblastic groove extends as shown in Pl. 15, fig. 18. In this figure it may be noted that the formative epiblast which lies above the primitive groove is thicker than that which bends round the edge of the keel. This illustrates the stretching of the formative epiblast, which reduces its thickness and causes it to approximate to the condition of the peripheral trophoblast.

Above the massive mesoblast on the anti-embryonic side of

the keel (i.e. the side opposite to the primitive streak) there is an indication of the linear splitting which precedes the formation of the exocœlom. On the embryonic side the mesoblast band is thicker, its nuclei lie at about three levels, and there is no distinct sign of the future splitting. The massive carinal mesoblast persists through some fifty sections of 10 μ . At last it comes to an end, and leaves the elongated apical region of the keel empty. The two mesoblastic bands then bend continuously into one another round the bottom of the hypoblastic groove (Pl. 15, fig. 19). They are generally two cell-layers in thickness with potential cœlom between the layers. More posteriorly there is a little interrupted splitting, giving rise to discontinuous spaces of incipient exocœlom.

Soon the mesoblast ceases and the hypoblast withdraws from the keel. The latter is now in section a very long and narrow trophoblastic process, composed of cubical epiblast, with its opposite walls touching each other in places, hanging freely into the placental groove. This posterior portion of the keel attains a depth of about 0.75 mm. Thus in this case there is a distinct trophoblastic keel-formation both in front and behind. In other words the two poles of the blastocyst are essentially alike; but there is this difference, that the obplacental adhesion is continued nearly to the extremity of the posterior pole.

VI. SUBSTAGE C.

This was cut from behind forwards, and numbered VIA in the Utrecht Catalogue. It was the first of the set of six early gestation sacs to be sectioned, and the preservation, staining, and mounting left little to be desired. But the series presented the apparent anomaly that whereas there was an exocœlom as well as a quantity of massive mesoblast, there was no obvious embryonic shield. Comparison with the other substages, the recognition of the primitive streak, and the excellent state of preservation showed that the apparent

absence of the formative epiblast which constitutes the embryonic shield was due to the general distension of the blastocyst and the elongation of the keel, whereby the thickened epiblast was reduced to a cubical epithelium.

Millimètres.

Height of gestation sac (i. e. total height of section, the mesometrium having been trimmed off)	10·00
Diameter of gestation sac	8·50
Height of cavum uteri	5·50
Depth of placental groove	2·50
Diameter of placental groove	0·50 to 0·75
„ omphaloid cavum	2·80
Thickness of placental mucosa	about 3·00
„ placental trophospongia	1·50
„ periplacental wall	3·90
„ obplacental wall	1·35

The anterior didermic extremity of the blastocyst is free, the posterior didermic pole is fixed by an abundant obplacental phagocytic contact with destruction of uterine epithelium. This occurs extensively also in the middle region of the blastocyst. Mitoses occur in the hypoblast and carinal trophoblast, but not in the obplacental trophoblast, where there are signs of amitosis. Here and there, embedded in the substance of the megalokaryocytes, a spherical mass of protoplasm is segregated from the surrounding cytoplasm and contains about a dozen small nuclei arranged in couples. In other cases the small nuclei appear to be budding from a meganucleus. I do not know the precise significance of these nests of small nuclei in the obplacental trophoblast, but they are not to be confused with the megalokaryocytes which are engaged in the ingestion of erythrocytes. Perhaps it is simply a means of adding, by amitosis, to the number of nuclei in the individual megalokaryocytes.

There is an extraordinary luxuriance of maternal capillaries at the denuded obplacental wall of the gestation sac, opening upon the trophoblast. There is no extravasation of blood

into the *cavum uteri*, but the capillaries actually abut upon the implanted megalokaryocytes and discharge their erythrocytes directly into the trophoblast. Consequently the megalokaryocytes are found commonly charged with half-dissolved blood-corpuscles. As mentioned there is no hæmorrhage; the extravasated erythrocytes are all contained in megalokaryocytes. In the posterior region of this blastocyst the whole of the upper third of the dome is implanted upon the uterine wall. Nevertheless the epithelial crypts at the mouths of the obplacental glands are not attacked by the trophoblast; phagocytic adhesion only occurs between neighbouring crypts, so that the obplacental union is a system of arcades, arching freely over the crypts. These are not like the pericarinal festoons which are miniature arcades not related to crypts.

Near the posterior pole the sections present a typical picture of a blastocyst with a deep trophoblastic keel, the hypoblast passing directly across the cavity without bending into it, precisely as already shown in Pl. 15, fig. 17, with the difference that in the case now under consideration the pole of the blastocyst does not lie freely in the *cavum uteri*, but is attached by a general obplacental implantation, skipping the mouths of the glands. Proceeding forwards we soon find the hypoblast dipping deeply into the keel, the distal walls of which are agglutinated together. At this level the blastocyst is didermic, there being no mesoblast in sight (Pl. 15, fig. 20).

As we approach the posterior V-shaped extremity of the mesoblast, we observe that the hypoblastic cells become loosened from their epithelial contiguity in the wall of the groove, but they do not escape into the cavity of the trophoblastic keel. This loosening of the carinal hypoblast occurs variously in all the substages; it would naturally be ascribed to defective preservation, but whether this would be correct or not, it certainly denotes a peculiar physiological modification of the hypoblast in this region (Pl. 15, fig. 21). Passing on, the mesoblast dehisces to form a spacious exocœlom, the

main cavity of which is lodged in the keel, while the narrow bands terminate in a solid proliferation or sinus terminalis on each side of the keel (Pl. 15, fig. 22).

About the plane of the posterior end of the mesoblast in the carinal region, the obplacental trophoblast changes its character in the coronal region. The megalokaryocytes are no longer implanted upon the mucosa, but present a free outer surface to the cavum uteri (Pl. 15, figs. 23 and 24). The large, evenly disposed cells contain numerous chromatic granules which they have ingested; similar granules occur in the uterine coagulum, and others are seen traversing the uterine epithelium. The special function of these modified megalokaryocytes is to ingest leucocytes whose nuclei yield and are composed of the granules in question. They occur over a continuous shield-like area of the coronal region of the blastocyst, and spread out forwards as the two pericoronal bands already mentioned (cf. Pl. 14, fig. 5). In some places the chromatophilous cells assume a flattened form as in Pl. 15, fig. 25.

The posterior exocœlom now requires a little extra consideration. It persists through some thirty sections and then gives way to massive tissue in the apical region of the keel, with cubical hypoblast flanked by narrow exocœlom dipping into it. In previous substages we have seen the commencement of the massive tissue of the keel at the posterior end of the primitive streak. In that part of its course where it is occupied by massive mesoblast I propose to designate the keel-formation, which appears like a stalk in section, by the term exostyle. When necessary the posterior exocœlom may be referred to briefly as the post-stylar cœlom. It is not merely post-embryonic in position, because the exostyle itself is post-embryonic.

As we follow the series forwards the exocœlom becomes greatly reduced, almost obsolete, and the massive keel actually adheres by its apex to one wall of the placental groove; this wall happens to be anti-embryonic, i. e. on the side away from the primitive streak. From the tip of the exostyle a cord of

slime is continued towards the bottom of the placental groove. It is noteworthy that where the hypoblastic groove of the omphalon penetrates into the carinal mesoblast, the epithelium retains a cubical character; whereas between this situation and the adcarinal membrane the hypoblast is loose. Another detail to be mentioned is that the uterine epithelium is not specially modified at the point of agglutination of the tip of the exostyle. It can hardly be doubted that the exostyle possesses a highly viscid surface, and the particular adhesion here described does not represent the position of the ultimate placental union (Pl. 16, fig. 26). In this connection it may be called to mind that in his monograph entitled 'Affen Ostindiens' (Wiesbaden, 1891, see p. 201), **E Selenka** found to his cost that the chorionic ectoderm (trophoblast) of *Semnopithecus* possesses a high degree of viscosity.

At the level of fig. 26 the chromatophagous layer of trophoblast still forms an uninterrupted calotte over the dome of the omphalon, and the corresponding portion of the uterine epithelium is intact. In the section from which the figure was drawn, two obplacental glands open into the coronal cavity. The granules which have been ingested by the trophoblast are commonly surrounded by what looks like a food-vacuole; this effect may be in part assignable to the bodies of the leucocytes (Pl. 15, fig. 25). A broad peripheral festooned zone of implantation occupies the widest portion of the omphalon, and uterine fluid can circulate through the trophoblastic arcades.

Twenty-six sections of $10\ \mu$ intervene between figs. 26 and 27. The nuclei of the exostyle present the appearance of being arranged in vertical rows or sheets. Mitoses are to be observed in the midst of the tissue as well as at the surface. The exostyle is marked off from the rest of the blastocyst by a geniculate bend due to increased resistance of its massive walls. It is penetrated throughout the greater part of its length by a central lumen continuous with the omphalon; the lining of this groove is not distinct from the rest of the stalk-

tissue except at its proximal or omphalad end. At the distal end there is a distinct trophoblastic space forming the cavity of the foot-like extremity which adjoins the uterine wall below the opening of a gland, the neck of which is undergoing occlusion by epithelial mitotic proliferation. Near the bottom of the placental groove the lumina of the glands cease before reaching the surface of the mucosa, the necks being blocked by a mixed tissue composed of its own degenerating elements and proliferating epithelial cells. The cubical trophoblast stops quite sharply at the top of the stalk in the figure. On the right of the figure a piece of the wall of the stalk is torn away and lies near the corresponding uterine wall without any jagged edge; nor is any jagged surface left upon the stalk where the detached piece belonged—a fact that accords with the sheet-like arrangement of the stalk cells mentioned above (Pl. 16, fig. 27).

The central lumen of the stalk (or exostyle) becomes interrupted in places as we trace it forwards, the tissue appearing solid in its central third, with a narrow chink in its distal third (Text-fig. 1). In this figure we see the swollen peripheral edges of the mesoblast, forecasting the sinus terminalis, and on one side only, namely on the embryonic side, a clear narrow exocœlom not extending into the stalk. The cubical trophoblast of the adcarinal wall of the omphalon stops short at the proximal bend of the stalk. A little farther on the stalk is solid throughout its central half, with proximal cavity continuous with the omphalon and a distal linear lumen terminated by a solid apex (Pl. 16, fig. 28).

The chromatophile trophoblast is now present at the sides of the dome, i. e. in the pericoronal region. In the centre of the dome there is a broad phagocytic contact with the denuded mucosa. The columnar uterine epithelium stands out with great prominence on either side of the denuded coronal area, while the broad equatorial zone of the omphalon shows very beautifully the pericarinal festoons (Pl. 14, fig. 5). It is a constant surprise to see normal uterine epithelium contiguous with a belt of implanted megalokaryocytes.

Between Pl. 16, figs. 28 and 29 there are fifty-four sections of $10\ \mu$. The central extension of the umbilical cavity has again become continuous throughout the greater part of the

TEXT-FIG. 1.



Section through mid-region of keel showing nearly solid exostyle.
 1. Sinus terminalis. 2. Exocoelom (on embryonic side). 3. Unsplit mesoblast (on anti-embryonic side). 4. Exostyle. 5. Trophoblastic apical cavity.

length of the exostyle. That part of the primordial sinus terminalis which is on the anti-embryonic side of the keel is now at the level of the geniculate bend. As before, the

cnical trophoblast ceases near the proximal end of the stalk. The nature of the cellular membrane which limits the surface of the exostyle is shown very clearly in fig. 29 near the distal end, where it is partly separated from the massive tissue. The solid mesoblast on the embryonic side of the central cavity of the exostyle is thicker than that on the other side. Below each section of the sinus terminalis a narrow exocœlom, very short on the anti-embryonic side, is visible.

On the anti-mesometric side of the *cavum uteri* the uterine epithelium at this level is complete except for a narrow area in the centre of the coronal region; the variously depressed chromatophile megalokaryocytes are stretched over the dome of the omphalon as far as the pericarinal zone where phagocytic contact is maintained.

The small cœlomic cleft noted on the anti-embryonic side below the *sinus terminalis* in fig. 29 is a local dehiscence in the mesoblast at that point. The mesoblast on this side becomes thinner, about two layers deep, as compared with six sheets of nuclei on the embryonic side. Great pieces become torn out of the embryonic side of the stalk, apparently owing to their adhesion to that side of the placental groove before preservation; the stalk as a whole is often much lacerated. The uterine muscles had presumably relaxed and so widened the groove after death. The blastocyst becomes quite free from the mucosa except at the two pericarinal angles. After about two dozen sections forwards from fig. 29, the exocœlom on the embryonic side begins to extend well into the stalk, none being present on the anti-embryonic side.

With the extension of the exocœlom into the exostyle on the embryonic side of the central hypoblastic cavity, we begin to recognise the position of the primitive streak at the distal end of the linear exocœlom; and it continues through some twenty sections. Close to the plane of the posterior end of the primitive streak a groove appears at the proximal face of the keel on the embryonic side. This groove persists through about ninety sections, and marks the peripheral

limit of the embryonic shield. At the same level a cœlomic space appears in the apical region of the keel beyond the distal end of the hypoblast. This is the pre-stylar exocœlom (Pl. 16, fig. 30).

We have now followed the massive exostyle throughout its entire extent between the post-stylar and the pre-stylar exocœlomic spaces. We have seen that it is never quite solid, there being always a trace of a linear hypoblastic axis. The position of the primitive streak marks the posterior boundary of the embryonic shield, which at first appeared strangely inconspicuous in this otherwise excellent series. The entire blastocyst is so well extended by the pressure of its internal fluid that the formative epiblast has become stretched, and so has suffered a diminution of thickness. This explanation is supported by the disposition of the nuclei, which are much more crowded on the embryonic than on the anti-embryonic side of the keel. The embryonic ectoderm consists of narrow cubical cells, the nuclei thus occurring in close juxtaposition; on the anti-embryonic side the trophoblastic ectoderm consists of flattened cells with distant nuclei (Pl. 16, fig. 30).

The anti-embryonic section of the primordial sinus terminalis passes definitely into the keel, becoming elongated in section (Pl. 16, fig. 31). Farther forwards it rounds the distal border of the carinal hypoblast, and finally meets its companion, which has meanwhile descended into the keel. In proportion as the two sections of the sinus terminalis approach their confluence, the cœlom dwindles to extinction (Pl. 16, fig. 32). After this the mesoblast ceases.

In front of the primitive streak it becomes difficult to determine with precision the distal limit of the embryonic shield, and its anterior border cannot be defined. In front of the mesoblast there are signs of ectodermal proliferation, especially in the vicinity of the proximal groove, which becomes deeper anteriorly. This is probably a proliferation of the annuogenic trophoblast. The growth of the obplacental trophoblast is accompanied by amitotic nuclear division, that

of the carinal trophoblast is effected by nuclear mitosis (Pl. 16, fig. 33, and Pl. 17, fig. 34).

In this anterior region the keel is didermic. Below the hypoblast there is a long narrow monodermic extension of the keel. The abrupt transition from cubical carinal hypoblast to flattened adcarinal hypoblast, shown on the anti-embryonic side in figs. 32 and 34, is a characteristic feature. It should also be mentioned, though not shown in the figures, that the flattened hypoblast of the adcarinal omphalopleure is separated from the adjacent trophoblast by a well-defined basement membrane, which stains strongly with orange G. In front of the region represented by these figures the proximal groove of the keel soon flattens out; the blastocyst appears free in the cavum uteri, and the anterior pole is reached.

VII. SUBSTAGE D.

This substage is rather poorly represented by a series of transverse sections cut from behind forwards and numbered VI E in the Utrecht catalogue. It may be considered to be characterised by the initiation of the lateral amniotic folds.

	Millimetres.
Height of gestation sac	11·00
Diameter " "	8·00
Height of cavum uteri	5·75
Depth of placental groove	2·50
Diameter of placental groove in middle	0·25
" " " near omphaloid end	0·50
Diameter of omphaloid cavum	3·00
Thickness of placental mucosa	4·00
" " trophospongia	2·00
" periplacental wall	4·00
" obplacental wall	1·00

Both poles of the blastocyst are fixed to the wall of the omphaloid cavum. Towards the posterior pole the adcarinal

omphalopleure was greatly folded, while the folding of the carinal trophoblast indicates the existence of a long keel like that shown in Pl. 15, fig. 17. As in the preceding substage, we first meet the posterior U-shaped solid end of the mesoblast, immediately in front of it the post-stylar cœlom, and then the massive exostylar tissue (Pl. 17, fig. 35).

This series is very useful for the migration of leucocytes from the mucosa, through the uterine epithelium and across the *cavum uteri* into the chromatophilous megalokaryocytes, as well as for the ingestion of erythrocytes by the phagocytic megalokaryocytes. The mechanism of ingestion of the leucocytes seems to consist of an active immigration, the megalokaryocytes, so long as they retain a free, unattached outer surface, remaining apparently passive. On the other hand the phagocytic activity of the implanted megalokaryocytes is often very obvious. Such cells, when engaged in the ingestion of red blood-corpuscles, commonly possess several large nuclei. The differentiation of the obplacental trophoblast into free leucocytophagous and attached erythrocytrophagous cells is a very singular and constant feature of the beaver's preplacental blastocyst.

In front of the region represented in Pl. 17, fig. 35, the carinal epiblast is ruptured, and this has led, over a certain extent of the series, to almost unaccountable confusion of the layers. It can be made out that the mesoblast becomes massed around the hypoblastic groove which dips into the keel as usual and is lined by cubical epithelium. The exocœlom becomes reduced to a linear cleft above the solid exostylar mass, and its walls may be in contact so that no open cœlom appears in the section. The carinal epiblast becomes greatly flattened, and there is an abrupt transition to the peripheral or adcarinal cubical epiblast (Pl. 17, fig. 36).

The rupture of the carinal epiblast noted in preceding sections culminates forwards in a notch at the apex of the keel. If such a section is examined apart from the rest, the bilobed apex of the keel might appear to have a special

bearing, whereas it is really an artefact. After a score of sections from the last one figured, the primitive streak can be recognised on one side of the keel not far from the free distal edge. Its position is approximately in the centre of the thickened formative epiblast which bends round the edge of the keel (Pl. 17, fig. 37). On the left side of the figure the formative epiblast is seen blending with the cubical adcarinal trophoblast; on the right it passes abruptly into what is left of the flattened epiblast of the keel.

The mesoblast continues to be massive on either side of the primitive streak. At the proximal end of the keel on the left side of the figure there is a small space limited externally by cubical mesoderm, internally by columnar mesoderm. I interpret this as part of the pericardial primordium, as will be explained more clearly below. As we pass forwards from this level the massive mesoblast gives way to open cœlom. In the anterior region of the embryonic shield the sections present the general appearance illustrated in Pl. 17, fig. 38. The keel is now embryonic; at its edges are seen incipient amniotic folds. The hypoblastic groove is cut tangentially near its anterior termination, and its carinal part appears separated from the omphaloidean hypoblast. Another part of the pericardial primordium is here seen in the mesoblast distad of the hypoblastic groove.

In front of the embryonic shield the anterior terminal portion of the exocœlom extends characteristically into the proximal half of the keel, leaving the distal half free (Pl. 17, fig. 39). Thus there is a very definite keel-formation near the anterior pole of the blastocyst, well in front of the embryonic shield.

The anterior and posterior trophoblastic portions of the keel with their exocœlomic spaces correspond in position with the ovate areas on the mature foetal sac which I described (1912, p. 203) as fenestræ pyriformes or umbilico-placental areas. Between the pre-stylar and post-stylar keels occurs the exostyle; between the anterior and posterior pyriform areas occurs the placenta.

VIII. SUBSTAGE E.

The series is cut transversely from before backwards, and is numbered VI_F in the Utrecht catalogue. There is notochordal contact between hypoblast and formative epiblast in front of the primitive streak.

	Millimetres.
Height of gestation sac . . .	about 10·00
Diameter „ „ . . .	7·60
Height of cavum uteri . . .	5·00
Depth of placental groove . . .	2·75
Diameter „ „ . . .	0·50 to 0·80
„ omphaloid cavum . . .	3·00
Thickness of placental mucosa . . .	about 3·00
„ „ trophospongia . . .	1·50
„ periplacental wall . . .	3·40
„ obplacental wall . . .	1·00

The anterior pole of the blastocyst exhibits phagocytic adhesion to the wall of the omphaloid cavum; the posterior pole is free. Beginning from the front end, we find a long keel composed of cubical epiblast with a hypoblastic groove dipping into the proximal part of its cavity. Distally the walls of the keel are agglutinated together so that the cavity is occluded. After about twenty sections of the formation just described, the mesoblast appears with a cœlomic cavity embracing the sides and bottom of the hypoblastic groove, with a long epiblastic keel beyond it. The hypoblastic groove is lined by cubical epithelium with large round nuclei. There is general phagocytic adhesion of the entire obplacental hemisphere in the anterior region.

At length the anterior end of the folded embryonic shield appears on the right side of the keel when the latter points towards the observer under the microscope (Pl. 17, fig. 40). Somewhat before this level is reached the coronal trophoblast begins to show patches of chromatophile cells alternating with phagocytic megalokaryocytes. This leads on to the condition of a continuous coronal chromatophilous calotte

such as has been described in previous substages, the leucocyte granules being extremely abundant. The mesoblast in the region of the embryonic shield is nearly solid, with a linear cleft representing the pericardial primordium.

Proceeding backwards with the sections, the solid mesoblastic bands become separated at a certain spot, and the embryonic hypoblast there comes into apposition with the formative epiblast, its cells at the same time acquiring a typical columnar form. It is the notochordal primordium (Pl. 17, fig. 41). This figure shows the solid peripheral swellings (*sinus terminalis*) of the mesoblastic bands placed at slightly different levels and a little exocœlom occurring between the swellings and the mass of the bands. The notochordal primordium extends through about a dozen sections of 10 μ , and then it passes into the primitive streak (Pl. 17, figs. 42 and 43). At this level of the blastocyst there is a very extensive megalocytic attack in the coronal region, flanked on either side by a pericoronal chromatophile band; beyond this there is a periomphaloid attack followed by pericarinal festoons — all in the typical manner previously described (cf. Pl. 14, fig. 5).

At the posterior end of the primitive streak the massive exostylar tissue commences and the mesoblastic bands enter into close contiguity with the carinal epiblast over a wide area (Pl. 17, fig. 44). The significance of the exostylar portion of the keel with its massive mesoblast and superjacent trophoblast (carinal epiblast) will be discussed below under "Special Considerations." In the mid-region of the exostyle in this series the keel is damaged in nearly every section in consequence of its having been torn from its viscid adhesion to the uterine wall. The figures are further complicated by the peculiar folding of the keel, which continues for some distance behind the embryonic shield (Pl. 17, fig. 45). Towards the posterior end of the exostyle the fold straightens out and we have the appearance shown in Pl. 17, fig. 46, where the massive tissue is bordered by a simple keel with juxtaposed walls. After this the post-stylar exocœlom opens

out in a typical manner (Pl. 18, fig. 47). Finally, the two sections of the primordial sinus terminalis meet together (Pl. 18, fig. 48), and thereafter the mesoblast ceases. Between the last two figures there are thirty-nine sections of 10 μ .

Behind the posterior limit of the mesoblast we find for some distance a didermic keel with trophoblastic extension (Pl. 18, fig. 49). The balloon-shaped blastocyst is here free from all adhesion to the uterine wall. Farther back, the hypoblast withdraws from the keel (Pl. 18, fig. 50), and eventually the section is exactly similar to that shown in Pl. 15, fig. 17, which relates to the anterior pole of the blastocyst in Substage B. The two poles of the blastocyst, though differing in the extent of their adhesion to the uterine wall, are naturally similar in other respects.

Apart from the broad difference between a free pole of the blastocyst and a fixed pole, there is another more subtle distinction which has been referred to incidentally and may be exemplified once more in this series, namely, the difference between a free and an implanted coronal disc. It may be noted in passing that the term "coronal" is not synonymous with "obplacental." The whole of the wall of the omphaloid cavum to which the omphaloid hemisphere of the blastocyst may be attached is obplacental. At the level of Pl. 17, fig. 44, the coronal region of the blastocyst in transverse section exactly equals the diameter of the field of the microscope when viewed under Zeiss oc. 4, obj. A; throughout this extent the denuded mucosa is lined by a continuous pseudo-epithelial sheet of megalokaryocytes closely attached by their amœboid peripheral ends to the decidual surface, without any arcades. At one edge of this implanted area, a gland opens into the pericoronal cavum at a true epithelial surface; at the other edge the pseudo-epithelium adjoins the true cylindrical epithelium of the pericoronal cavum of that side. The implanted trophoblast does not sink into the mucosa; in general the line of implantation is straight, corresponding to the original basement membrane of the

uterine epithelium. The subepithelial capillaries, at frequent intervals, where they come into contact with the trophoblast, actually open and discharge their red corpuscles directly into individual megalokaryocytes. The obplacental glands almost always open at an epithelial surface subtended by a trophoblastic arcade, but in a few rare instances a gland is seen to open directly upon the trophoblast, into which it discharges a mass of intrusive chromatic granules. At the level of fig. 47, instead of the implanted pseudo-epithelial coronal trophoblast, we find the coronal region of the blastocyst entirely free, composed of chromatophilous megalokaryocytes, as represented diagrammatically in Pl. 15, fig. 24.

IX. SUBSTAGE F.

This excellent series shows very clearly the embryonic shield with primordia of medullary groove, notochord, pericardium and amniotic fold. It is cut from before backwards and is numbered VI c in the Utrecht catalogue. Both poles of the blastocyst are fixed to the wall of the omphaloid cavum.

	Millimetres.
Height of gestation sac	10·00
Diameter of gestation sac	8·00
Height of cavum uteri	5·00
Depth of placental groove	2·00
Diameter of placental groove	0·75 to 2·00
,, omphaloid cavum	3·00
Thickness of placental mucosa	4·00
,, ,, trophospongia	2·00
,, periplacental wall	3·50 on one side, 4·00 on the other.
,, obplacental wall	1·00 to 1·35

These measurements, taken in conjunction with Pl. 18, fig. 51, exhibit a placental groove which is considerably wider and shallower than anything that has gone before. This progressive expansion of the cavum uteri accords with

the fact that the blastodisc is farther advanced in development, though the exostyle is still far from its destination on the placental trophospongia. The estimated length of the blastocyst is nearly 4 mm.

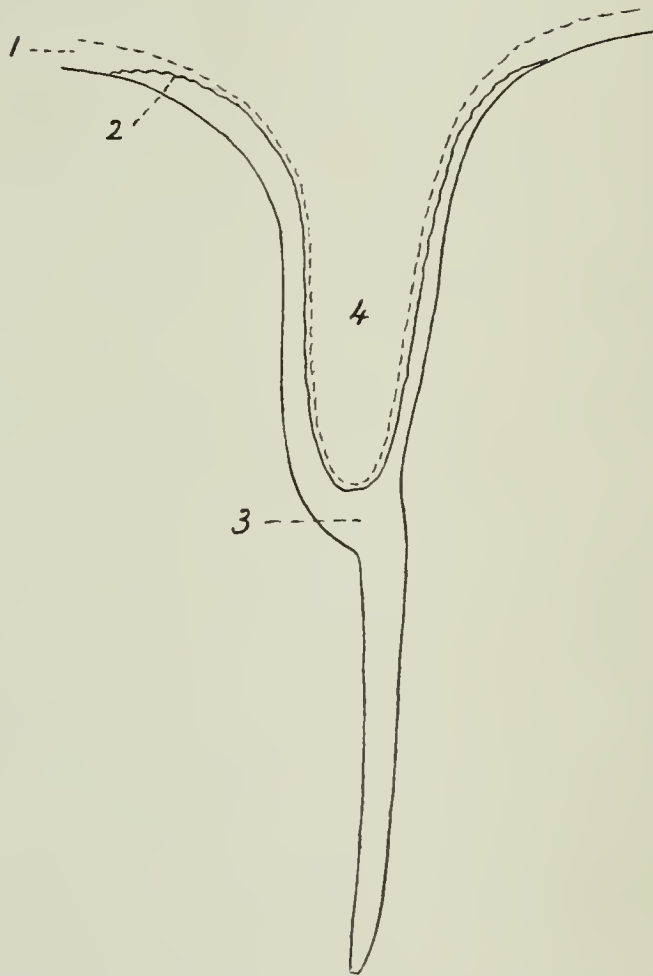
At the anterior pole the blastocyst is monodermic, and is attached by the omphaloid hemisphere in broad arcades. Then the hypoblast appears a short distance removed from the pole; at first it stretches straight across the adcarinal plane and a little further back dips down into the proximal half of the keel, the distal half of which remains monodermic. In previous substages it has been observed that in places, the epithelium which lines the hypoblastic groove, i. e. the carinal hypoblast, tends to break up into rounded cells that lie loosely in the cavity of the groove, but never escape into the distal cavity of the keel. The extent and position of the hypoblastic groove can always be made out, however disconnected its cells may be. This fact is due to the peculiar behaviour of the basement membrane which exists between the adcarinal epiblast and hypoblast.

At a certain point near the mouth of the keel the adcarinal basement membrane can be seen to cross the narrow interval that separates the epiblast from the hypoblast, and to attach itself to the latter, which it accompanies into the keel. The trophoblastic cavity of the keel is thus shut off from the omphalon by a delicate wrinkled membrane. The keel-cavity contains a finely granular coagulum, which differs slightly in its staining properties from the adjacent coagulum in the adcarinal region, so that there is a sharp contrast in the character of the coagulum on either side of this structureless membrane (Text-fig. 2). The membrane is inconspicuous and easily overlooked.

The anterior border of the mesoblast appears on one side of the keel, viz. the embryonic side, as shown by subsequent sections. In this region there is a remarkably deep epiblastic keel extending far beyond hypoblast and mesoblast (Pl. 18, fig. 52). The mesoblast rapidly increases in volume as we trace it backwards, and presently the anterior cœlom opens

out with a deep extension into the keel. Produced beyond this carinal cœlom there is a rather long and somewhat folded epiblastic keel with its walls agglutinated so as to occlude the potential trophoblastic cavity.

TEXT-FIG. 2.

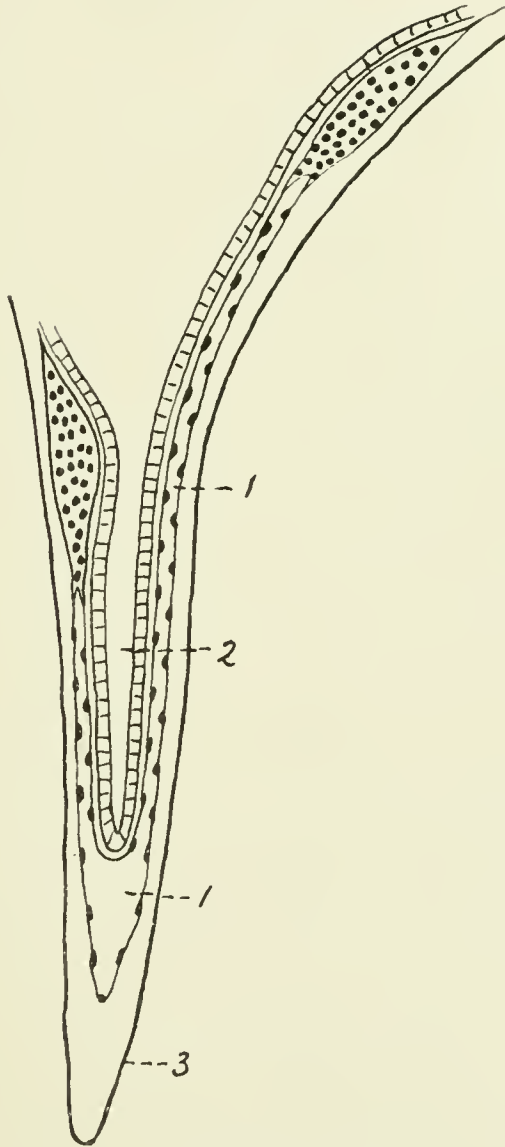


Anterior region of keel, showing relation of basement membrane to carinal hypoblast. 1. Interval between hypoblast and epiblast containing adcarinal coagulum. 2. Basement membrane crossing the interval to join the carinal hypoblast. 3. Trophoblastic cavity of keel. 4. Hypoblastic groove.

The epiblastic keel soon begins to shorten, the carinal cœlom becomes reduced, and the cells of the hypoblastic groove appear as a continuous epithelium on the embryonic side. In the diagram (Text-fig. 3) I have reconstructed the

hypoblast on the anti-embryonic side of the keel, where it is evanescent in the actual section. Between the condition

TEXT-FIG. 3.



Appearance of the keel behind the anterior polar region. The index numbers are placed on the embryonic side of the keel.
 1. Exocoelom. 2. Hypoblastic groove. 3. Shortened epiblastic keel.

shown in Pl. 18, fig. 52, and that in Text-fig. 3 there are thirty-nine sections of $10\ \mu$. At the region of the blastocyst which we have now reached the coronal disc is composed

of large chromatophile cells freely subtending the coronal cavity, which is filled with coagulum containing many chromatic granules. Two or three sections after Text-fig. 3, the front part of the embryonic shield begins to be cut tangentially. Its abrupt appearance in section indicates a much sharper definition than in previous substages.

Under the Zeiss microscope, when the keel appears to point towards the observer, the embryonic shield is placed on the right side of the keel. The plate-drawings were reversed under the Edinger apparatus. For descriptive purposes we may regard the edge of the keel as pointing downwards towards the observer, although it really points upwards towards the mesometrium. Above the embryonic shield in the figure (Pl. 18, fig. 53) there is a somatopleuric fold which looks like a lateral amniotic fold and is so interpreted. Below the shield in the figure there is the epiblastic keel into the neck of which the exocœlom of that side is produced, so that the material for the other amniotic fold is in continuity with the keel. Underneath the thick formative epiblast of the shield we find a thick-walled mesodermic sacculle, interpreted as the pericardial primordium of the embryonic cœlom. The only cœlom at present existing in the embryo is the pericardial cœlom. Against this the embryonic hypoblast consists of a continuous cubical epithelium, while on the opposite side the hypoblast is evanescent and granular. Below the distal border of the hypoblast a thin sheet of mesoblast intervenes between it and the epiblast (Pl. 18, fig. 53).

Proceeding backwards, the pericardial sacculle shortly separates into two moieties. The portion which lies subcentrally under the thickened epiblast shows a characteristic thicker inner wall of columnar cells and a thinner outer wall of cubical cells. Between the two parts of the pericardial cœlom the mesoblast thins out, and so the cubical hypoblast comes nearer to the formative epiblast at this point (Pl. 18, fig. 54). The next figure shows an accentuation of the preceding features, and is introduced to exhibit the

two diverging limbs of the pericardial cœlom which now appear as antimeres (Pl. 18, fig. 55).

As we approach the posterior quarter of the blastodisc, the embryonic shield becomes larger, and a medullary groove with subjacent notochordal plate appears in the position shown in Pl. 19, fig. 56. After another half-score sections we have the structure represented in Pl. 19, fig. 57. The medullary groove and the distal pericardial process have ceased, and the lower part of the keel begins to be occupied by massive mesoblast with a hypoblastic diverticulum extending into it. At the foot of the keel there is an open hollow space containing coagulum; it is possible that it is an incident of growth rather than that it has any special significance, but this may remain an open question. In this figure and the preceding, the sinus terminalis is seen low down on the anti-embryonic side of the keel; on the embryonic side it occurs near the junction of the adcarinal and carinal regions. This unequal behaviour of the parts of the sinus terminalis has been observed in all substages.

At the posterior end of the blastodisc, the primitive streak in this substage is reduced both in extent and definition, and it is evident that it would soon be given up. Its position and the wings of massive mesoblast proceeding from it are shown in Pl. 19, fig. 58. The hypoblastic groove lined by cubical epithelium intruding into the distal mesoblast is conspicuous, and the transition from cubical to flattened epithelium is remarkably abrupt.

We are now rapidly nearing the region of the massive exostyle which always follows behind the primitive streak. In this substage the exostyle exhibits in section a broad distal base with a small trophoblastic cavity and hypoblast penetrating into the massive mesoblast. The epiblast on one side of the keel is peculiarly folded. The distal lumen of the hypoblastic groove is occluded, the occlusion taking place by opposition of the walls accompanied by intense proliferation of the massive mesoblast, whereby the axial hypoblast merges imperceptibly with the surrounding mesoblast, without the

intervention of a basement membrane (Pl. 19, fig. 59). The large clear nuclei of the intrusive tongue of hypoblast contrast with the more darkly stained mesoblastic nuclei in their normal aspect, but they appear to blend with the latter at the sides and apex. On the anti-embryonic side of the keel there is unsplit mesoblast; on the embryonic side an exocœlom whose epithelium is partly cubical. The anti-embryonic part of the sinus terminalis lies low down, midway between the foot of the keel and the position of the sinus on the embryonic side. The massive tissue of the exostyle is concentrated within somewhat narrow bounds, covering about a dozen sections of $10\ \mu$. This concentration and delimitation of the exostyle are what must necessarily precede the initial discoplacental adhesion.

A few sections behind Pl. 19, fig. 59, the axial cavity reappears in the hypoblast and this marks the transition from the exostyle to the post-stylar region. A deep and narrow hypoblastic groove occupies the centre of the mesoblast; above the massive tissue the exocœlom opens out on both sides to form a wide cavity. Below the mesoblast there is a trophoblastic extension of the keel (Pl. 19, fig. 60).

At the region of the blastocyst corresponding approximately with the course of the exostyle, the obplacental wall exhibits the condition of a continuous megalocytic attack accompanied by ingestion of red corpuscles in the coronal area, and a wide pericoronal arcade subtending a pericoronal cavum on each side. As already explained, the term arcade in this connection expresses typically a single bridge of chromatophilous trophoblast with free outer surface washed by the uterine fluid. The particular function of the obplacental arcades, in addition to the ingestion of leucocytes by the chromatophile cells, is to afford spaces for the openings of the persistent obplacental glands.

Posteriorly the two halves of the exocœlom unite to form a common cavity, the post-stylar cœlom, which extends some way into the distal cavity of the keel (Pl. 19, fig. 61). After this the trophoblastic keel lengthens enormously (Pl. 19, fig. 62).

About this region of the blastocyst the sections show demonstratively the ingestion of erythrocytes by the coronal megakaryocytes and the ingestion of leucocytes with their lobed chromatic nuclei by the pericoronal chromatocytes. In addition to the coronal implantation and the pericoronal cava, there is a typical periomphaloid adhesion and pericarinal festoons.

The two sections of the sinus terminalis descend deeper into the keel, and finally come near to each other at the bottom of the carinal hypoblast as shown in Pl. 19, fig. 63, which is thirty-nine sections behind the preceding figure. At the same time the post-stylar cœlom is reduced, and the trophoblastic extension of the keel is devoid of a continuous axial lumen. In Pl. 19, fig. 64, the two parts of the sinus nearly touch; and fig. 65 shows the sigmoid confluence of the sinus, marking the posterior limit of cœlom and mesoblast.

Next follows the posterior didermic region of the blastocyst. The trophoblastic keel shortens, but the hypoblast retains its carinal extension until near the posterior pole. These features, as well as the relation of the keel to the adcarinal omphalopleure, are portrayed in Pl. 20, fig. 66. Quite at the posterior pole we find in section a round didermic blastocyst free on its mesometric side, adhering intermittently elsewhere.

X. MATERNAL TROPHOSPONGIA.

Without undertaking a detailed discussion of the histology of the mucosa, attention may be invited to certain interesting changes which take place in the uterine mucosa of the gestation sac, preliminary to placentation. The perusal of the foregoing pages will doubtless have left a vivid impression of the vital importance to the beaver's blastocyst of its obplacental implantation. One might have expected, from the analogy of the rabbit, that this would involve the degeneration of the obplacental uterine glands. On the contrary, the obplacental glands retain their full func-

tion throughout the period dealt with, and the trophoblast gives free way to their crypt-like openings. It is only in the walls of the mesometric or placental groove, which have not yet entered into very close association with the blastocyst, that the glands have already become atrophic.

The mucosa may be regarded as comprising two classes of tissue: (1) Uterine epithelium and glands; (2) dermatic connective tissue and capillaries. The fixation of the blastocyst resolves itself into two periods: (1) Preplacental period; (2) euplacental period. The size of the gestation sac is determined by two factors: (1) Dermatic proliferation; (2) pressure of blastocyst.

In one of the uterine cornua belonging to a later phase of gestation which will be described below, there was a slightly swollen segment of the uterus, which looked as if it might contain a very young blastocyst. After it had been sectioned, it was found to be in a perfectly healthy condition, but non-gravid. This series is numbered VII x in the Utrecht catalogue. The *cavum uteri* is a rather narrow lumen bifurcated towards the mesometrium and lined by a high columnar epithelium; opening into it on all sides there is a profusion of glands (Pl. 20, fig. 67). It contains a coagulum with some dark-stained granules diffused throughout it. The lumen is invested outside the epithelium by a narrow uniform zone of intense dermatic proliferation riddled with capillaries; in this zone (not indicated in the figure) the connective-tissue cells are more numerous and closer together than in the deeper parts of the mucosa. On the mesometric side the lumen branches into two grooves, separated by a ridge or dermatic cone covered by epithelium. Numerous large vessels occur between the circular and longitudinal muscles of the mesometric region; the circular muscle-ring is broad and entire, except where penetrated by the vessels.

In contrast with the initial condition of uniform dermatic proliferation and intact glands described above in a non-gravid segment, we find in a gravid gestation sac belonging to the preplacental period that all the mesometric and peri-

placental glands are undergoing necrosis, being met and vanquished by an epithelial proliferation operating centrifugally. The dermatic proliferation acts centripetally. Meanwhile the dermatic proliferation in the future placental region has outstripped the remainder, and now constitutes what has been referred to as the placental trophospongia, the term "trophospongia" having been introduced by **Hubrecht** in 1889 to denote a vascular maternal proliferation. In the beaver such a proliferation takes place all round the *cavum uteri*, and is at first of uniform thickness.

The epithelial proliferation is a phenomenon of substitution accompanying the necrosis of the glands. It is paralleled by a corresponding phenomenon described by **Hubrecht** (1893) in the case of the shrew (*Sorex*), where the epithelial proliferation leads to the formation of secondary crypts. In the beaver's gestation sac during the preplacental period, the placental mucosa, towards the bottom of the placental groove, exhibits, sometimes very clearly, radiating bands of necrotic glands, with dark-stained shrunken nuclei (Pl. 20, fig. 68). These glands are to be replaced by an extensive epithelial proliferation, which grows centrifugally into the substance of the placental trophospongia in the form of two lobulate wings, which correspond in their position with the grooves on either side of the dermatic cone in the non-gravid uterus (Pl. 20, fig. 67). Thus the wing-like epithelial proliferations are preceded by necrotic belts. The cells multiply by mitosis. In the niches between the lobes are found subepithelial capillaries (Pl. 20, fig. 69).

In the obplacental region, where the subepithelial capillaries are also excessively abundant, the capillaries are conveyed by the centripetal dermatic proliferation. This happens in the placental region as well, but in addition the centrifugal epithelial proliferation descends to meet the capillaries and embrace them, thereby preparing a nidus for the true placental implantation. At the beginning, the proliferating cells retain their cell-boundaries (Pl. 20, fig. 70). Eventually the proliferation will become syncytial. At the level

of the anterior part of the embryonic shield in substage F, the capillaries which adjoin the inner borders of the wing-like mesometric proliferations are greatly dilated, but there is no trace of any endothelial proliferation (Pl. 20, fig. 71).

At the distal borders of the two principal mesometric proliferations there are to be seen traces of the glands which they have supplanted. There are no signs of glands between the wings; the latter cause the more laterally placed mesometric glands to diverge widely, arching round the mesometric area, appearing healthy in their deep-lying portions, but failing to reach the surface, their neck-portions having been killed. Sometimes a transverse section of a glandular tube is seen, the centripetal half of which is necrotic, the distal half normal. In this way, centripetal glandular degeneration and centrifugal epithelial proliferation take place simultaneously. In the obplacental region the glands persist and the uterine epithelium is largely replaced by trophoblast; in the placental region the glands degenerate and are replaced by epithelial proliferations which are to some extent moulded upon the pre-existing glands. At the sides of the placental groove the necks of the glands sometimes widen out into large ampulliform dilatations with ill-defined walls and wrinkled nuclei; such ampullæ fail to open into the *cavum uteri*. They may nearly open, but their mouths are blocked, partly by their own degenerate cells and partly by epithelial cells (Pl. 20, fig. 72).

There is not much to add to what has been said already regarding the uterine epithelium. Where the trophoblast is free and the epithelium consequently intact, the character of the latter varies at different points without any regard to symmetry. In one instance my notes record an epithelium so flattened as to become a pavement epithelium, covering the left side only of the omphaloid *cavum*. The cytoplasm of the uterine epithelium stains dark yellow with orange G, and thus offers a marked contrast to the adjoining trophoblast, whose cytoplasm remains pale. J. W. Jenkinson (1902, p. 132) has noted the same distinction in the case of the mouse:

“The cytoplasm [of the trophoblast cells] does not stain intensely with acid stains, and may in this way be readily distinguished from the cytoplasm of the maternal cells.” Again, on p. 139, referring to epithelial cells which have been ingested by the trophoblast, he says: “As for the cytoplasm, it stains brilliantly with plasma stains, and offers in this respect a marked contrast to the cytoplasm of the trophoblast by which it has been ingested.” This last is true of the erythrocytes ingested by the megalokaryocytes in the beaver.

There are signs that in the beaver the uterine epithelium may not only disappear by direct substitution of the trophoblast in situ, but that, in a manner not unlike what **P. Nolf** (1896) described in the bat, it may first be reduced to a cubical and then to a pavement epithelium; or finally it may, in places, be shredded off into the cavum uteri.

The migration of leucocytes from the mucosa across the uterine epithelium into the omphaloid cavum and thence into the chromatophilous megalokaryocytes, or, more briefly, chromatocytes, is a phenomenon that requires further comment. Granules staining darkly with hæmalaun, occurring commonly in triads and tetrads, are found deep down in the stroma of the obplacental mucosa. From the deeper zone they scatter through the intermediate stratum and are again met with in great numbers in a subepithelial position, from whence they pass into the epithelium. At first I supposed that they might be derived from the nuclei of the decidual cells, but was unable to find transitional forms. Not only do they traverse the uterine epithelium, but they also pass in smaller quantities into the lumina of the glands, and are then discharged with the glandular secretion into the cavum uteri. In much less numbers are they observed in the capillaries.

In places the obplacental mucosa showed an abundant infiltration of undoubted leucocytes whose lobed nuclei were these same chromatic granules of whose nature I had been uncertain. When they reach the bases of the epithelial cells and penetrate through the latter, their cytoplasm does not

stain so well as it does in the middle of the mucosa, but remains clear so that the granules often appear to be contained in vacuoles. When they arrive in the uterine fluid, which is represented in the sections by a coagulum staining deeply with orange G, the cell-body is often invisible though sometimes quite obvious. The marked tendency which they exhibit to discharge themselves in volleys through the uterine epithelium corresponds with their deep-seated gregarious habit in the mucosa. This infiltration of leucocytes is comparable with that observed by Nolf in the epithelioid tissue and hypertrophied venous endothelium of the bat's trophospongia, although their fate is different.

XI. DISCOPLACENTAL ADHESION.

The stage of the incipient placentation is unfortunately lacking in the material collected by me. In the keel of the preplacental blastocyst four parts with independent destinies may be distinguished: the anterior keel with anterior exocœlom, the embryonic keel, the exostyle, and the posterior keel with post-stylar exocœlom. The first and last will be employed in the formation of the umbilico-placental membranes or fenestræ pyriformes, consisting of diplotrophoblast, i. e. trophoblast doubled by the somatic mesoblast of the exocœlom. The embryo will become folded off, and will sink with its amnion into the exocœlom. The exostyle will furnish the material for the placental labyrinth.

But the chapter recording these events in their actuality cannot yet be written. The groove at the foot of the keel in Pl. 19, fig. 59, is ready to receive the dermatic cone of the maternal trophospongia with its syncytial caps (cf. Pl. 20, figs. 69-71), but we are not at present privileged to witness the act.

XII. THE ESTABLISHED PLACENTA.

The material upon which the following description is based consisted of six spherical gestation sacs about 25 mm.

in diameter, obtained on two separate occasions—March 4th and March 10th, 1913. It was on the latter date that I also obtained the six youngest gestation sacs. In a female beaver, taken on March 4th, there were two spherical swellings, each 25 mm. in diameter, in the left uterus only, and two contiguous corpora lutea in the left ovary. Above the upper swelling there was a smaller one of 12·5 mm., upon which great hopes were set; but it proved barren. The axillary teats of the mother were distinct, but the post-axillary pair was only found after the skin had been removed. The trapper said it was a young female that would have been three years old in the coming spring. In another female, taken on March 10th, there was a single spherical sac in the left uterus, and three in the right. From these data it may be gathered that whilst the beaver produces a litter only once a year in the spring, there is a considerable range of variation with regard to the stages which may be observed upon a given date during the season of reproduction.

I opened one of these sacs in Prof. Hubrecht's presence by slicing away the antimesometric wall with a cartilage knife. We were surprised to find that no liquid exuded when the cavity of the omphalon was exposed; on the contrary it was entirely filled by a translucent coagulum which cut like cheese and showed no tendency to break away. One slice, about 2 mm. thick, was cut through the middle of the gestation sac; the coagulum, stretched from wall to wall like a sheet of gelatine, retained its position exactly, and the cut surfaces remained flat.

In the mesometric half the embryo could be seen through the coagulum lying on one side, its left side being presented towards the omphalon. The embryo lies in the exocœlon between the placenta and the umbilical membrane. The minimum thickness of the uterine wall exceeded 4 mm.; the maximum was nearly 6 mm.; the diameter of the *cavum uteri*, and consequently of the omphalon that occupied it, was about 12 mm. (Pl. 20, figs. 73 and 74). The placenta, measured in section, had a length of 4·25 mm., and a height

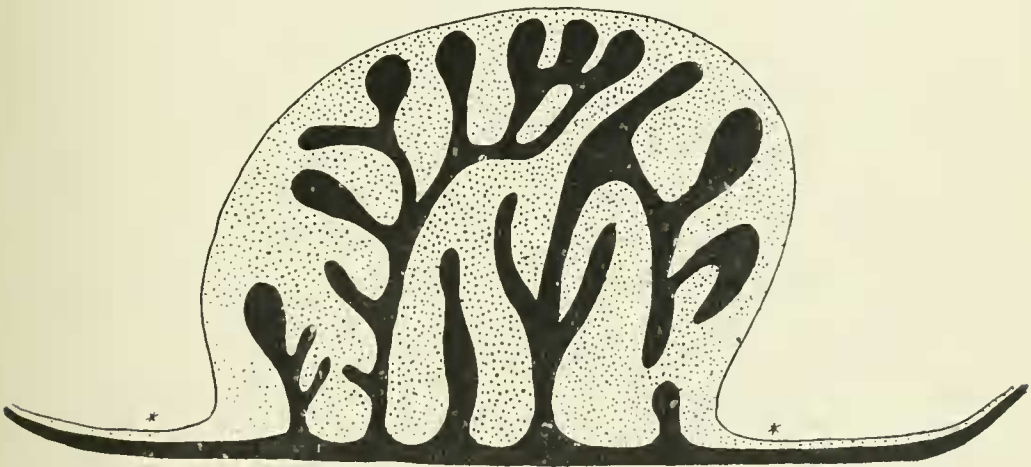
of 2.25 mm. The latter measurement signifies that the somewhat mushroom-shaped placenta projected freely to that extent into the exocoelom. After being reduced to sections the body of the embryo was found to have shrunken rather badly owing to the treatment it had received. When the destination of such early stages is the microtome they should not be cut open previously. Fortunately there was no lack of good material.

In its shape and projection the placenta may be likened to a cushion or a mushroom or a dome. At its edge it overlaps the base of insertion, so that in sections passing tangentially through the margin it appears detached from the uterine wall. Such tangential sections are useful for determining the essential structure of the placental labyrinth. There is a straight trophoblastic base continuous with the rest of the trophoblastic wall of the blastocyst, from which centripetal trabeculæ ascend into the allantoic mesoblast. These trophoblastic trabeculæ are excavated by canals which carry maternal blood, and are what **M. Duval** called sanguimaternal lacunæ in the ectoplacenta. The allantoic mesoblast conveys foetal capillaries to the placental labyrinth. The allantoic tissue appears in the form of centrifugal villi interlacing with the centripetal trabeculæ, together establishing the placental labyrinth (Text-fig. 4). Neither the trophoblast nor the allantoic mesoblast remains passive in the growing placenta, but they grow in opposite directions, the trophoblast centripetally, the allantoic mesoblast centrifugally.

After passing the point where the placenta is inserted into and united with the uterine wall, the definite basal layer of trophoblast with its sharp demarcation disappears. Wherever the trophoblast touches allantoic tissue it is composed of a cellular layer corresponding to what **E. van Beneden** (1888) called the cytoblast, subsequently lengthened into cytotrophoblast by **J. H. Vernhout** (1894). Towards maternal blood and trophospongia the trophoblast presents a plasmodial layer termed "plasmodiblast" or "plasmoditrophoblast." For the sanguimaternal lacunæ in the trophoblastic trabeculæ

the plasmodiblast furnishes a pseudo-endothelium. The solid buds produced at the growing edge of the placenta consist of cytoblast which ascends into the allantoic tissue. The cytoblastic buds anastomose and so enclose allantoic islands. The cytoblast is the formative layer of the trophoblast; it may be compared with the Malpighian layer of the skin, but instead of giving rise to horny cells on its outer surface, it produces plasmodiblast which is rooted in the vascular trophospongia. The cytoblast itself is rooted in the vascular allantoic tissue;

TEXT-FIG. 4.



Section through growing margin of placenta. Trophoblast black, mesoblast dotted. The asterisks indicate the line where the allantoic and somatic tissues meet; outside the asterisks the double membrane is diplotrophoblast.

it does not give off any buds towards the maternal tissue. The cytoblast is a growing tissue, the plasmodiblast is a feeding organ, and the trophospongia is the nidus supplying the nutriment.

The foregoing aphorisms are indited with special reference to the conditions observed in the beaver, but they derive support from the observations of others upon different animals. In the rabbit, **H. Schoenfeld** (1903), confirming **Maximow**, states that the plasmodiblast is supplied with elements from the cytoblast, and adds that it has no growth of its own; it moves about upon the surface of the cytoblast

as described by **A. Maximow** (1900). In the squirrel (*Sciurus*), **F. Muller** (1905, p. 560) says that the growth of the placenta does not take place merely by the substitution of foetal for maternal tissues, but by the progressive centripetal growth of the ectoplacental mass, which thus surrounds the allantoic villi more and more; nevertheless the greater part of the uterine mucosa is supplanted by the placenta, because a continual process of degeneration and resorption of maternal tissue is taking place.

In the bat, **P. Nolf** (1896, p. 610) says that the increase in thickness of the placenta is not the result of peripheral growth at the expense of the maternal tissue. Almost all of its secondary growth is centripetal; the internal or foetal face of the placenta grows towards and projects into the blastodermic cavity. This is proved by the fact that the vegetative epiblast throughout gestation is continued into the placental cytoblast, not at the level of the internal surface of the placenta, but at the level of its external surface. This conclusion accords, he says, with those deduced by **Duval** for Carnivora, by **Hubrecht** for the shrew, and by **Vernhout** for the mole.

In all these instances the nutritive material for the centripetal growth of the ectoplacental trophoblast is furnished by the maternal trophospongia, which forms a cushion upon which the placenta rests. In the beaver this trophospongia has a twofold origin in a vascular dermatic proliferation and a lobular epithelial proliferation. The latter is now broken up into polygonal blocks by the capillary network, producing an areolated structure in section. Many of the epithelial areolæ have degenerated into syncytia in which numerous dark-stained nuclei are densely aggregated. Sometimes a syncytial mass is extensive and then there appears a curved band of nuclei in the midst of it. The epithelial areolæ, the syncytia, and the aggregations of deeply staining nuclei are very characteristic of the early trophospongia of the beaver's placenta. To these features should be added the presence at certain points of brown granules chiefly surrounding large

degenerating maternal nuclei. In the deeper zone of the maternal trophospongia the cell-islands are not yet syncytial; some are entirely cellular, others are partly syncytial.

There are interesting analogies between events in the pre-placental and euplacental periods, as under :

Preplacental period.	Euplacental period.
1. Uterine glands partly normal, partly necrotic.	. Epithelial areolæ partly cellular, partly syncytial.
2. Centripetal dermatic proliferation conveying maternal capillaries.	. Centrifugal allantoic proliferation conveying foetal capillaries.
3. Centrifugal epithelial proliferation into the dermatic tissue.	. Centripetal ectoplacental proliferation into the allantoic tissue.

At the junction of trophoblast and trophospongia a symplasma is formed. **Schoenfeld** (1902) discusses the use of the terms syncytium and plasmodium which were introduced by Prof. **Haeckel**; and symplasma suggested by Graf **Spee**. A syncytium is immobile, a plasmodium is mobile. In connection with the phenomena of placentation, **Schoenfeld** applies syncytium to maternal formations, plasmodium to foetal formations. Only when the foetal plasmodium comes into contact with the maternal syncytium does the latter undergo degeneration and become converted into a symplasma which is defined as a syncytium in retrogression. The symplasma is brought about by the incorporation of maternal protoplasm and nuclei into the substance of the plasmodium. Until the degeneration of the maternal elements is complete, the peripheral zone of the plasmodium is a symplasma containing active foetal nuclei and passive maternal nuclei. This interpretation involves perhaps a slight extension of the original meaning of the term symplasma. In the dog, **Schoenfeld** described the fusion of decidual cells with the plasmodium, thus converting the latter, for the time being, into a mixed "foeto-maternal plasmodium"; but there can be no harm in calling it a symplasma.¹ Good illustrations of a typical symplasma in the sense here indicated were

¹ To avoid possible ambiguity perhaps the term "symplasmodium" might be preferred.

given by **A. Maximow** (1900, Taf. xxx, figs. 1 and 2) for the rabbit.

At many points the junction of plasmodium and syncytium is rendered conspicuous by the presence of the crowded syncytial nuclei, which contrast in colour, size and shape with the smaller, paler, oval, and more evenly distributed plasmodial nuclei. The conjoint symplasma may be observed to surround superficial capillaries of the trophospongia together with adjoining decidual cells. At such places the plasmodial nuclei may be seen intruding into the syncytium, and no boundary can be drawn between the plasmodial protoplasm and the syncytial protoplasm. The inclusion of maternal capillaries seems to be effected by the tortuous growth of the allantoic tissue which pushes the trophoblast before it into the trophospongia, so that we find in the border zone between trophospongia and placental labyrinth islands of allantoic tissue surrounded by trophoblast, and outside that a mantle of symplasma (Pl. 20, fig. 75). In the diagrammatic figure (Pl. 20, fig. 76), the allantoic villi, with their trophoblastic investment, are seen to be tipped by syncytial groups of nuclei, rendered in black. The characteristic trophospongiol islands or areolæ show, in the sections, various grades of syncytiation at different levels, there being no regularity in the distribution of the syncytia throughout the trophospongia, except at the symplasma or zone of contact.

The trophospongiol islands, whether syncytial or cellular, are separated by capillaries with normal endothelium. At the base of the trophospongiol cushion, between it and the massive dermatic proliferation, there is a basal sinus-like blood-space, to which large capillary vessels pass vertically through the dermatic tissue from the direction of the mesometrium. This arrangement is indicated in Pl. 20, fig. 76. Near each pole of the placenta a large vessel is found receiving its affluents from the sanguimaternal lacunæ in the swollen tips of the trophoblastic trabeculæ; from thence it descends into the mucosa. The two polar vessels possess a proliferated endothelium which they retain until they reach a point deep in the

mucosa, where each of them is continued into a narrow vessel with normal endothelium which passes directly and abruptly into the proliferated walls (Pl. 20, fig. 77). There is an equally abrupt transition from the proliferated endothelium to the plasmodial pseudo-endothelium near the foetal periphery of the placenta. At one pole the vessel penetrates the placenta near its right margin; at the other pole it enters near the left margin.

The data at my disposal do not permit of a direct comparison of the placental circulation of the beaver with other types which have been investigated. Such comparisons should be made at equivalent stages. The circulation in the early established placenta will necessarily differ in its details from that in the mature finished placenta. As for the latter, excellent figures have been given by **Tafari** of the injected placenta of various mammals, less successful perhaps as regards the rabbit, but remarkably clear as regards rat, guinea-pig, and bat. The placenta of the guinea-pig possesses its own special features. That of the rat (*Mus decumanus*), as represented in **Tafari's** tav. v, fig. 2, is more like that of the bat (*Vespertilio murinus*, tav. vi, fig. 2) than the guinea-pig (Tav. v, fig. 1). In *Mus* and in *Vespertilio* there is a central maternal artery penetrating through the middle of the discoplacenta to its foetal aspect, where it spreads out into the afferent sanguinamaternæ lacunæ.

To left and right of the placental insertion the areolated trophospongia merges imperceptibly into a marginal zone of hollow crypts, the walls of which are partly necrotic. In the obplacental and periplacental regions of the gestation sac the dermatic cells constitute an epithelioid tissue comparable to Nolf's epithelioid layer in the bat. In the mesometric region the dermatic tissue, though proliferating, still retains a primitive aspect, and does not present an epithelioid mosaic pattern in section.

Median sections through the placenta show that the dermatic tissue in which the vessels are lodged projects like a

cone into the trophospongial cushion (Pl. 21, fig. 78). After leaving the basal trophospongial sinus, which now appears as an arched line between the dermatic axis and the areolated cortical substance, the vessels branch and enter into numerous anastomoses with each other, forming a rete mirabile within the dermatic cone continuous with the trophospongial sinns, which is itself retiform. With a simple lens the trophospongial crescent with its peripheral zone of syncytia, its interstitial meshwork, and its basal sinus, can be seen to perfection following the contour of the dermatic cone with its rete mirabile.

Another series, cut nearly longitudinally through the gestation sac, showed the placenta in a slightly more advanced condition—4.50 mm. in length, 3.75 mm. high. In tangential sections, i. e. such as do not pass through the central trophospongial cone, the allantoic mesoblastic villi penetrate deeply and tortuously into the embryotrophic cap of areolated trophospongia, so that allantoic islands, surrounded by their trophoblastic investment, appear in section amongst the areolæ.

Towards the centre of the placenta, the concentric strata of which it is composed stand out very clearly. Beginning at the foetal aspect, there is first a narrow zone of allantoic mesoblast containing the superficial allantoic vessels; then the swollen ends of the trabeculæ dilated with the sanguinomaternal lacunæ; thirdly, the labyrinth of anastomosing trabeculæ; fourthly, the border zone of symplasma; fifthly, the trophospongial areolæ; sixthly, the dermatic cone. Most of these parts are to be found in figures already referred to, and again in Pl. 21, fig. 79. Since the polar vessels enter the placenta near its right and left margins, neither of them is seen in a median section. Noteworthy is the abrupt transition from the areolated trophospongia to the dermatic tissue.

The position of the embryo in the blastocyst conforms to the rule which applies to those Vertebrates in which there is a great disparity between the animal and vegetative poles, i. e. when an omphalon or a yolk-sac is present. It has been

mentioned above, and the figures show, that the umbilical membrane or *area vasculosa* stretches across the foetal sac midway between placenta and obplacenta. The body of the embryo, surrounded by its amnion, lies sideways in the exocœlom between placenta and umbilical membrane, with its right side towards the placenta and its left side towards the omphalon (Pl. 20, fig. 73, and Pl. 21, fig. 79). In the Sauropsida, at the gill-slit or branchiotrematic stage, the embryo also comes to lie with its left side towards the yolk-sac. In the rabbit, at the same stage, the forebody of the embryo by reason of the cervical flexure projects into the umbilical vesicle surrounded by the proamnion, or, more precisely, the proamniotic omphalopleure. In the beaver there is no trace of a proamnion at this stage; and when it is remembered that in the preplacental blastocyst the mesoblast is continuous within the circuit of the sinus terminalis, except at the notochordal contact, and that there exists already an anterior as well as a posterior median extension of the exocœlom, the formation of a proamnion at any stage would seem to be excluded.

In Pl. 21, fig. 79, we see the amniotic membrane stretching between the umbilical membrane and the placenta. In the same figure the opening of the omphalomesenteric duct into the omphalon and that of the allantoic canal into the flattened allantois are indicated, though they do not occur actually on the same section. The allantoic canal communicates with the hypoblastic cloaca, into which the Wolffian ducts now open, and forms the hypoblastic axis of a mesoblastic stalk, accompanied by two arteries and a vein. At the distal end of the stalk the canal widens out as the allantoic sac which is imbedded in the thickness of the mesoblast at the foetal surface of the placenta, causing no protuberance. This flattened sac has a longitudinal extension of about 0·75 mm. During part of its course from the cloaca to the sac, the lumen of the allantoic canal is occluded by cellular proliferation, so that it becomes solid; this condition has been observed in two series.

In one series (VII A in the Utrecht catalogue) the omphalomesenteric duct has a partially occluded lumen; but in another series (V B) the lumen is open, and contains maternal blood-corpuscles, which it conveys from the omphalon to the mid-gut. The presence of red blood-corpuscles in the mid-gut could not easily be attributed to accident, and it appeared at first a mystery how they came to be there. The clue to the mystery was found in the behaviour of the obplacental trophoblast, which at this stage consists of flattened megakaryocytes closely applied to the uterine wall; here and there they are greatly distended with erythrocytes, and there is evidence of the transfusion of maternal corpuscles into the omphalon. They pass into this cavity across the obplacental trophoblast, and are in fact to be found scattered in the midst of the coagulum.

I will conclude this chapter with some further details concerning the embryo in order to define the stage of development which it has now reached with greater precision. Its actual age cannot be estimated, and can only be roughly guessed at. If we assume the period of gestation to be one hundred days, then these embryos will certainly fall within the first twenty-five days, and probably within the first fifteen days; the preplacental blastocysts are likely to belong to the first ten days. The relative age is best reckoned according to the size of the gestation sac.

The embryo is now in the gill-slit or branchiotrematic stage; the mouth is open, but there is no anus. In section the mouth-cavity, flattened dorso-ventrally, appears like a pair of gill-slits, but this is entirely deceptive, since the formation is that of the stomodæum with its pituitary diverticulum meeting the blind end of the infundibulum. The four pairs of true gill-pouches just fail to open to the exterior, being closed over externally by a narrow cellular bridge. The auditory sacs are closed; the optic stalk is hollow, the optic cup and choroid fissure are formed, and the lens invagination is still connected with the ectoderm. Suitable sections show a length of the spinal cord flanked by

somites resembling the corresponding figure of a 12 mm. pig embryo in **C. S. Minot's** 'Laboratory Text-book of Embryology,' p. 230, fig. 135. The buds of the fore-limbs are rather more advanced than those of the hind-limbs, which appear as broad crescentic thickenings.

XIII. INTERMEDIATE STAGES.

Two stages, intermediate between the establishment of the growing placenta and the final period towards the term of gestation when it ceases to grow, were obtained, but have not yet been worked out in section. Their external characters present two points of special interest concerning the early relations of the chorion l ave or diplotrophoblast of the umbilico-placental areas, and the appearance of a spherical allantoic vesicle. At the stage described in the preceding chapter, the allantois occurred as a narrow tube communicating proximally with the cloacal region and expanding distally into a flattened sac immersed in the allantoic mesoblast at the surface of the placental labyrinth, not causing any additional protuberance into the exoc elom.

The next older stage is represented by three gestation sacs, one in the right horn of the uterus, two in the left. These were despatched to me in a tin containing 10 per cent. formalin on March 23rd. The swellings were equal, somewhat shrunken, 60 mm. in long diameter. Upon cutting through the antimesometric wall, 2.50 mm. thick, the umbilical membrane (*area vasculosa*) was seen to be expanded and in contact with the mucosa, though devoid of attachment. Along the courses of the vessels low ridges are developed, which press against the mucosa, so that the impressions of the larger vessels are distinctly visible upon the smooth inner surface. When first opened the mucosa appeared dark reddish and spongy, with white giant-cells showing against the ground colour when viewed under a simple lens.

When the foetal sac was cut into, the umbilical membrane was found to be adherent to the amnion, from which it could be peeled off. In the mesometric division of the foetal sac the amniotic membrane bends inwards to its insertion upon the dome of the placenta, and here it becomes free from the umbilical membrane, so that a considerable exocœlomic cavity exists in this region. Thus the baggy amnion hangs loosely in the mesometric exocœlom, but elsewhere adheres by simple contact to the area vasculosa, obliterating the exocœlomic cavity. A linea alba marks its insertion upon the placenta.

By slicing away the wall of the gestation sac, which becomes thicker (5 mm.) towards the mesometrium, and then removing a portion of the vascular membrane, the foetus, 38 mm. long, is exposed, loosely enveloped by the spacious amnion. On the mesometric side, the area vasculosa ends with a villous rim at the two connecting membranes which surround the aditus of the interuterine segments. In this region the mucosa presents a rugose or convoluted surface, and the folds are continued as opaque whitish buttresses from the mucosa to the connecting membranes, extending as far as the edge of a narrow clear zone below the villous rim of the umbilical membrane. At this stage, therefore, simple dissection suffices to demonstrate the dual composition of the definitive connecting membrane (Pl. 21, fig. 80).

On laying open the whole cavity of the exocœlom the polar areas of the foetal sac are exposed from the inside. They cover over the aditus of the interuterine segments. The dissection was made shortly after the preservation in formol, and the polar areas (umbilico-placental areas) appeared as clear, non-vascular membranes forming turgid protuberances into the exocœlom near each end of the placenta, each being surrounded by part of the sinus terminalis. The pyriform caudad protuberance was 9 mm. high, 10 mm. long; the convex cephalad protuberance was about 5 mm. high by 11 mm. long (Pl. 21, fig. 81). In another specimen opened several months later the polar areas were flattened

out. In fig. 81 the caudad end of the foetal sac is also the caudad end of the gestation sac; the head of the embryo is directed towards that segment of the uterus which leads to the Fallopian tube. The cephalad protuberance lies over the opening or aditus of that segment, while the caudad protuberance arches over the posterior opening. The placenta measured 33 mm. in length, 21 mm. in width, and 21 mm. in height. Besides its remarkable form and bold eminence, the most noticeable feature was the absence of an allantoic vesicle. The position of the allantoic sac at the placental surface was indicated by a flat membrane without fluid, situated beyond the centre of distribution of the vessels. In a second specimen from the same tract there was a very small incipient allantoic vesicle with a transparent wall. In both of these instances the head of the foetus was directed towards the oviduct.

The next intermediate stage is represented by four gestation sacs, one right and three left, sent to me in 10 per cent. formalin on April 6th, having an average length of 81 mm. Soon after the arrival of the material I opened all the sacs by cutting out an obplacental piece from each, and punctured each vascular foetal sac, collecting the clear fluid that squirted out. The amnion was again closely adherent to the umbilical membrane, so that in puncturing the latter the amnion was also pierced, and the clear fluid, which appeared faintly straw-coloured *en masse*, was the liquor amnii. In the later stages, when the foetus has nearly attained its limit of growth, the amnion loses its adhesion to the umbilical membrane, so that the exocœlom then becomes the main cavity of the foetal sac. At the present stage the amniotic cavity is the main cavity of the foetal sac, the exocœlom, even to the base of the placenta, being temporarily obliterated.

The wall of the gestation sac has now become reduced to a mean thickness of about 2 mm. In the first specimen examined the head of the foetus was again directed towards the Fallopian tube. The foetus as it lies in its amnion has a

length of 73 mm., measured from the crown of the head to the base of the tail. The flattened tail is not bent under the body, but simply curves round against the posterior end of the foetal sac, extending a little beyond the hind feet; it measured 15 mm. in length. The placenta now has a length of 42 mm.

The most conspicuous difference between this and the preceding stage is the presence of a spherical allantoic vesicle, about 16 mm. in diameter, with thin pellucid wall, projecting boldly into the amniotic cavity. It lies just in front of the centre of distribution of the allantoic vessels into the placental labyrinth (Pl. 21, fig. 82).

The three gestation sacs in the left uterus held their foetus in the following positions: In the one nearest to the ovary the head of the foetus is directed towards the cervix uteri; in the middle sac the foetus lies in the same position, with the head towards the cervix; in the last of the three, i. e. the one nearest to the vagina, the head of the foetus is directed towards the oviduct, the tail towards the cervix.

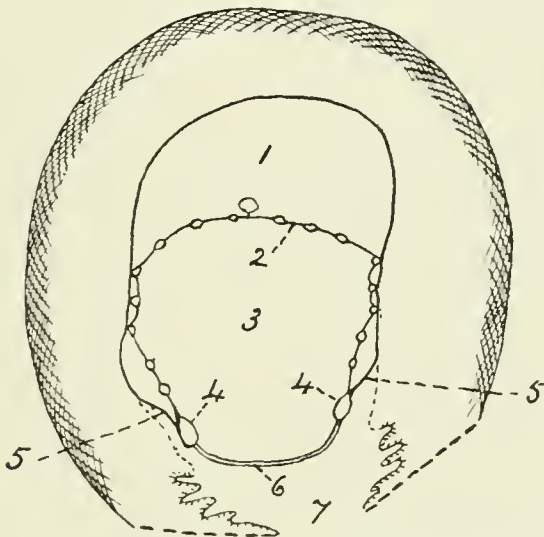
XIV. THE CONNECTING MEMBRANE.

At the early placental stage represented in Pl. 20, fig. 76 and fig. 79, the umbilical membrane is invaginated about halfway into the omphalon and stretches like a diaphragm across the blastocyst, separating the omphalon from the exocœlom. The latter is limited towards the aditus of the gestation sac by a sheet of somatopleure or diplotrophoblast, which constitutes one of the umbilico-placental areas described in my former paper (1912). At the poles of the foetal sac, beyond the range of the placenta, this membrane stretches free across the cavum uteri within the circuit of the sinus terminalis (Text-fig. 5).

From the outer edge of the sinus terminalis two other membranes arise—the umbilical membrane and the omphalopleure. The short free zone of omphalopleure intervening between the sinus and the uterine wall is the primordial

connecting membrane. It is clearly derived from the adcarinal membrane of the preplacental blastocyst; it is what is left of this membrane after the peripheral encroachment of the primordial area vasculosa has ceased. It continues to grow in later stages, and, by accession of material from the uterine mucosa, becomes converted into the definitive umbilico-uterine connecting membrane. The latter is therefore a composite membrane of dual origin,

TEXT-FIG. 5.



Section through region of one of the aditus of the gestation sac at the early placental stage. 1. Omphalon. 2. Umbilical membrane. 3. Exocoelom. 4. Sinus terminalis. 5. Connecting omphalopleure (representing adcarinal membrane). 6. Diplotrophoblast. 7. Aditus.

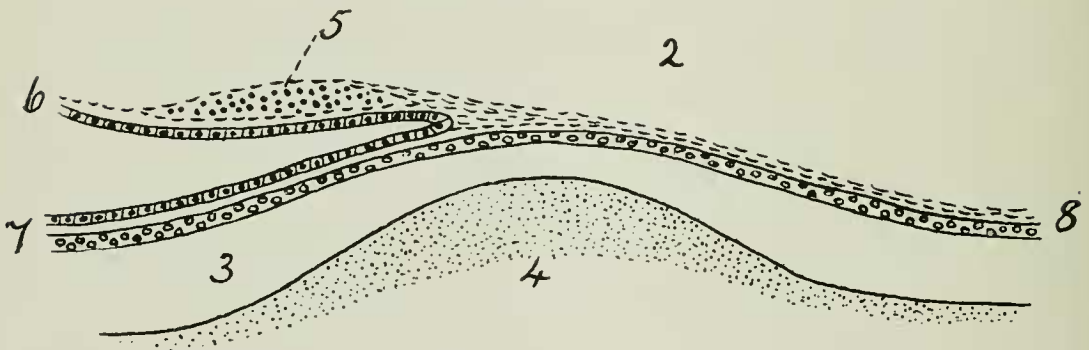
as was indicated in the preceding chapter. This fact is proved by its early history as well as by its histological structure, into the details of which I will forbear to enter at present, although illustrations have been prepared. The manner of junction of splanchnopleure, omphalopleure and somatopleure at the level of the sinus terminalis in the early placental stage is shown in Text-fig. 6.

From the earliest to the latest days of placentation the sinus terminalis is situated at the junction of the three membranes whose primary names have just been given. Their

secondary designations are respectively—umbilical membrane, umbilico-uterine membrane, and umbilico-placental membrane.

The omphalopleure, as a whole, constitutes the inferior (anti-mesometric) wall of the omphalon and of the entire blastocyst. It is present in all its integrity during the early placental period but disappears in later stages, with the exception of the persistent connecting membrane. The origin of the latter is thus explained. It is a secondary product of the primary obplacental implantation of the

TEXT-FIG. 6.



Part of periplacental wall of blastocyst, at the early placental stage, to show the junction of membranes at the sinus terminalis. 1. Cavity of omphalon. 2. Exocoelom. 3. Cavum uteri. 4. Mucosa. 5. Sinus terminalis. 6. Splanchnopleure. 7. Omphalopleure. 8. Somatopleure.

blastocyst, and directly comparable with the adcarinal omphalopleure of the preplacental blastocyst. The umbilical membrane forms the major part of the outer wall of the mature foetal sac. In my former paper on the beaver (1912, p. 207) I called it the vascular chorion or endochorion of the rodent blastocyst, not being at that time aware of the circumstance that the more suitable name, umbilical membrane, had been applied to it for the rabbit by **E. van Beneden** and **C. Julin** in 1884.

The umbilico-placental membrane is in its origin a non-vascular somatopleure or diplotrophoblast, but in the mature foetal sac there are intrusive capillaries proceeding into it

from the area vasculosa. They form anastomosing loops, and bear a resemblance to the capillary loops in the chorion l ave of the bat's blastocyst as figured by van **Beneden** and **Julin**.

The reason for the existence of the connecting membrane which supplements the placental implantation in the attachment of the foetal sac to the gestation sac, may perhaps be sought in the semi-aquatic habits of the beaver and in the fact that the female retains her activity, leaving the lodge and swimming under the ice to procure food from the submerged stock of winter-provender, throughout the period of gestation. Were it not for the additional support afforded by the connecting membrane, the narrow deciduous root of the massive placenta might easily be torn asunder. The connecting membrane must relieve the placenta of much of the stress and strain to which it would otherwise be exposed.

The nearest approach to the condition of having a connecting membrane seems to be represented by a temporary formation, which was described in the early gestation sac of *Sciurus* by **F. Muller** in 1905. It appears that the periplacental mucosa forms a ring-shaped thickening to which the thickened trophoblast adheres before the folding of the amnion. In the following stage this ring-shaped zone of implantation, with the sinus terminalis close to it, continues to extend, leaving the placental part of the cavum uteri still unoccupied, but with numerous crypts opening into it.

In the young gestation sac of *Sciurus*, when the blastocyst is attached to the obplacental wall, the cavum uteri, as had been previously observed by **Fleischmann**, becomes constricted by a circular periplacental thickening into a smaller mesometric and a larger anti-mesometric portion. The zone of adhesion or omphalo-placental ring ("omphaloiden placentatiering," **F. Muller**, *op. cit.*, p. 395) occurs at the lip of the mesometric cavum. In this ring an epithelial syncytium is formed, with which the trophoblast becomes intimately united. At length the syncytium is destroyed and

then the plasmodial union is exchanged for simple adhesion. Later still even this is given up. This early periplacental implantation occurs at the level of the sinus terminalis, and is interpreted by **Muller** as a vestigial omphaloid placentation such as had not been described in rodents before. The periplacental connection has nothing to do with the allantoic placenta which forms subsequently. It extends below and thus embraces the openings or aditus of the gestation sac. Its limited centripetal growth and its transitory endurance are its most remarkable features.

There can hardly be a doubt that the temporary omphaloplacental adhesion of *Sciurus* is comparable with the permanent umbilico-uterine connection of *Castor*.

XV. SPECIAL CONSIDERATIONS.

The two leading characteristics of the preplacental blastocyst of the beaver, the obplacental implantation with differentiation of erythrocytrophagous and leucocytrophagous megakaryocytes, and the placental keel, are of specific physiological importance to the growing embryo, but they also have a comparative value which can only be elucidated by a brief discussion. In order that the reader may be orientated with regard to the systematic position of the beaver, a few words of introduction are desirable.

Although the beaver, in structure and habits, is unique amongst the Rodentia, displaying in high degree the qualities of intelligence and adaptability to local conditions, yet it would be wrong to suppose that it is farthest removed from a primitive organisation. On the contrary, in its monotrematous cloaca and pentadactyle limbs, to mention these two external features only, it retains the marks of a very ancient mammalian type. In my former paper (1912) it was suggested that "the beaver occupies a position amongst Rodentia comparable with that attained by man amongst primates." It is well known that man has retained some primitive features in limbs, teeth and digestive tract, as compared with many other

mammals. Just as **Hubrecht's** discovery of the blastocyst of *Tarsius* with its "Haftstiel" indicated an excessively remote origin for the primate ontogeny, so the blastocyst of the beaver with its exostyle may have an analogous bearing upon rodent ontogeny.

It is generally agreed, under the support of such authorities as **Cope**, **Winge**, and **Tullberg**, that the beaver family is related to the squirrel family, both of these families being associated under **J. F. Brandt's** suborder, *Sciuromorpha* (1855). **Tullberg** divides the *Simplicidentata* into two great tribes, *Hystricognathi* and *Sciurognathi*. The latter comprises two sub-tribes, *Myomorphi* and *Sciuromorphi*; and the latter falls into three sections, *Sciuroidei*, *Castoroidei*, and *Geomyoidei*. **Winge** (quoted by **Tullberg**) held that rodents are to be derived from primitive *Mammalia* resembling the least specialised *Insectivora*, from which they diverged by cumulative increase of the gnawing habit.

F. Muller (1905), adopting **Haeckel's** (1895) generalisations maintained that of all Rodents the *Sciuromorpha* have diverged least from the ancestral type; and he added that the genus *Sciurus* in particular occupies the most central position and has preserved the most primitive form. On the other hand, **Max Weber** (1892) regarded the scales on the tail of the beaver as the remains of a primitive scaly covering of the body.

The preplacental blastocyst of *Lepus* and *Sciurus* is a plano-convex blastocyst, that of *Mus* and *Cavia* is an inverted blastocyst, that of *Castor* is an everted blastocyst. The task before us is not to decide which of these three is the most primitive type of blastocyst, but to consider which of them offers the readiest comparison with the blastocyst of *Tarsius*. It may be premised that in one respect the euplacental blastocyst of the beaver is the most primitive known amongst existing Rodents by reason of the persistence of the umbilico-uterine connecting membrane which is a consequence of the periplacental implantation of the trophoblast.

The keel extends from end to end of the elongated balloon-shaped blastocyst, along its superior or mesometric side, dipping into the deep placental groove. One of the fundamental relations of this remarkable formation is so obvious that its importance in establishing the reality of the phenomenon might escape attention—namely, the coincidence in the configuration of the wall of the blastocyst and that of the *cavum uteri* or cavity of the gestation sac. The keel may thus be accepted at once as a fact, and need not be regarded with suspicion as an artefact.

There are four or five principal structures concerned in the constitution of the keel: the epiblastic keel, the mesoblastic keel, the hypoblastic keel and the embryonic keel, to which may be added the exocœlomic keel. The interpretation and comparison with other forms will hinge upon the massive mesoblastic keel which follows behind the primitive streak. It is convenient to anticipate conclusions to some extent by assuming that the keel represents an ancient or primitive mechanism, and that the exerted mesoblastic keel of the beaver is comparable with the "Haftstiel" of *Tarsius*, monkeys and man.

History of the "Haftstiel."—So far as I have been able to ascertain, the first use of the term "Haftstiel" as applied to the mammalian blastocyst occurs in *Selenka's* memoir on the opossum (1887, vide his text-fig. C, on p. 136 *op. cit.*). In this case the main cavity of the blastocyst is the omphalon, into which the allantoic vesicle, surrounded by a narrow exocœlom, hangs freely. In the early Primate blastocyst the main cavity is the exocœlom, into which the reduced omphalon hangs freely. These conflicting relations depend upon the varying degrees of development of the exocœlom, allantois and omphalon respectively. In the opossum the embryo with its allantoic vesicle and exocœlom is suspended from the chorion or wall of the fœtal sac into the main cavity (omphalon) by a hollow exocœlomic stalk. In the Primates the embryo with its umbilical vesicle is sus-

pended from the chorion into the main cavity (exocœlom) by a massive allantoic stalk. There is no massive allantoic mesoderm in the opossum and no hollow allantoic vesicle in man. Just as the term "chorion" is often used to denote the wall of the foetal sac, irrespective of the constitution of its membranes, so the term "Haftstiel" denotes the mechanism by which the embryo is suspended within the cavity of the foetal sac.

The real knowledge of the Primate "Haftstiel" dates from **His's** third memoir on the 'Anatomie Menschlicher Embryonen' (1885). I have not seen the original memoir, but the subject is treated very fully by **C. S. Minot** in his contribution entitled "Uterus and Embryo" (1889). **His** made what **Minot** appraised as "the discovery of fundamental importance"—that in the early human blastocyst the allantoic sac appears as a small endodermic tube lying in a posterior prolongation of the body which **His** called the "Bauchstiel," and that at this early stage the allanto-chorionic vessels already run to and branch out upon the chorion. Thus "the allantois is, from the first, continuous with the chorion" (**Milnes Marshall**, 1893).

F. Keibel has stated recently (1913) that the allantoic tube in the human blastocyst is an entirely vestigial structure; he does not say explicitly of what it is a vestige, but the text implies clearly that he considers it to be a vestige of the free allantoic vesicle of Sauropsida. The beaver may help us to another explanation, namely, that it is a vestige of that portion of the omphalon which descends into a keel-shaped "Haftstiel" or exostyle. The latter term can be used in general as an equivalent rendering of "Haftstiel," its etymology being analogous to that of exocœlom, both terms referring to structures that lie outside the embryo.

Selenka's memoir on the "Affen Ostindiens" appeared in 1891. In this monograph it was shown that the characteristics of the monkey's blastocyst are: (1) The early separation of the omphalon ("yolk-sac") from the chorion; it takes no part in the nutrition of the embryo and must be regarded as a

vestigial structure; it is scantily supplied with vessels and floats as a small stalked vesicle in the exocœlom, until by the expansion of the amnion it becomes pressed against the chorion and finally succumbs to resorption.

(2) The spacious exocœlom acts as a reservoir of food-stuffs until the allantoic vessels take over the function of foetal metabolism.

(3) After the formation of the amnion (the method of which was not observed), the embryo retains its connection with the placental chorion by a solid cord of mesoblast into which a rudimentary allantoic tube penetrates. This massive cord with its vestigial endodermic cavity is the allantoic stalk or "Haftstiel," the vehicle of the placental vessels.

(4) The main cavity of the early blastocyst is the exocœlom. Subsequently the amniotic cavity dilates enormously and the amnion finally fuses with the chorion, so that the cavity of the foetal sac is then amniotic cavity.

From the above résumé it is obvious that **Selenka's** "Haftstiel" is identical with **His's** "Bauchstiel." As an English equivalent the expression "body-stalk" has been suggested by **C. S. Minot** and adopted by **J. W. Jenkinson**; but if the comparison with the beaver is accepted, the need for a more general term, e. g. exostyle, is indicated.

We must now refer briefly to **Hubrecht's** classical paper in **Gegenbaur's 'Festschrift'** (1896), entitled "Die Keimblase von *Tarsius*." The chief characteristics of the *Tarsius* blastocyst may be summarised:

(1) Rauber's layer, or the trophoblast over the formative epiblast, disappears in the very early stages, shortly after the delamination of the hypoblast.

(2) The exocœlom has a remarkably precocious development and the hypoblastic sac occupies only a small portion of the spacious blastocyst.

(3) The blastodisc is at first excentric. The ectoplacental proliferation of the trophoblast is situated some way behind the blastodisc, not diametrically opposite to it.

(4) Between the ectoplacental proliferation and the posterior

border of the blastodisc (embryonic shield), there extends a solid mesoblastic tract which at the same time forms part of the wall of the closed mesoblastic sac or exocœlom; this solid cord is the "Haftstiel." At this stage there is no mesoderm in the embryo and the region of the embryonic shield is still didermic.

(5) The blastocyst is only attached to the uterine wall by the ectoplacental disc; otherwise it lies free in the uterine lumen.

(6) A complete and close-meshed area vasculosa develops in the wall of the hypoblastic sac or umbilical vesicle, and is filled with blood-corpuscles long before the heart begins to beat; but vascular rudiments arise in the "Haftstiel" before the appearance of the omphaloidean network.

(7) The mesoblast of the "Haftstiel" is at first contiguous with the adjacent trophoblast; but, *pari passu* with the formation of the amnion, it becomes separated from the trophoblast by insinuation of the exocœlom and so becomes converted into the primordial umbilical cord.

(8) After the "Haftstiel" has become vascularised and enlarged, a tubular outgrowth from the umbilical vesicle penetrates backwards into the connective tissue of the "Haftstiel." This is the allantoic diverticulum of the umbilical vesicle.

From this brief tabulation of **Hubrecht's** discoveries regarding the blastocyst of *Tarsius*, we gather that although the allantoic tube is a secondary outgrowth, it belongs to the omphalon. There is no question of its being a diverticulum of the hind-gut at its first origin. Again, the "Haftstiel" is directly continuous with the primitive streak, and forms, at the beginning, part of the wall of the blastocyst behind the embryo. In 1889 **Hubrecht**, à propos of *Erinaceus*, had defined the "Haftstiel" as a caudal mesoblastic cord which grows backwards from the posterior end of the primitive streak in order to promote the early vascularisation of the chorion. To this definition **Resink** (1904) added in italics: "Der

Haftstiel entsteht jedoch als die von Anfang an vorhandene Verbindung des entypierten Keimfeldes mit dem Chorion."

In the preplacental blastocyst of the beaver, the endodermic allantois does not appear as an outgrowth, but is actually a deep hypoblastic groove of the omphalon extending into the keel. It is, therefore, from the first an integral part of the omphalon. The steps by which this hypoblastic groove becomes narrowed down to the allantoic canal with its distal flattened sac cannot be followed in the material at my disposal. It must take place simultaneously with the closure of the digestive tract of the embryo, which is similarly associated with the narrowing down of the omphalomesenteric duct.

With reference to the above quotation from **Resink**, a pupil of **Hubrecht**, the important point in my estimation is his insistence upon the primary character of the "Haftstiel," which is not in its essence a secondary formation (cf. **Milnes Marshall**, 1893). The flattened "Haftstiel" of *Tarsius* may be directly compared with the keel-shaped exostyle of the beaver. Both of these structures are organs of fixation, by means of which the embryo attaches itself to the placental complex. The ectoplacental disc is derived from the proliferation of the exostylar trophoblast. The localisation of the "Haftstiel" in *Tarsius* and the exostyle in the beaver affords strong confirmation of the view put forward by **Minot** in 1889, that the discoidal placenta is probably a primitive placental type. The chief characteristic of the blastocyst of *Castor* is the possession of a massive keel-shaped exostyle or "Haftstiel" into which the endodermic allantois extends as a primary groove of the omphalon; and the exostyle itself is directly continuous with the proliferation of the primitive streak. In his useful, though doubtless ephemeral, speculations concerning the origin of the foetal annexes of Mammalia, **Resink** admitted that he was unable to explain the origin of the allantoic sac. Perhaps the beaver may offer a new point of view from which this problem may be envisaged.

Within the limits of the order of the Rodentia, the conditions preceding the ectoplacental implantation of the beaver's blastocyst are most readily compared with those obtaining in squirrels. According to **Fleischmann** (1893), in *Spermophilus*, where there is no preplacental keel, the gestation sac is none the less subdivided into an omphaloid cavum and a discoid placental cavum or "Scheibenhöhle." The young blastocyst is attached in the omphaloid cavum, and is so orientated that the embryonic pole (blastodisc) lies over the narrow passage (called "Schlossspalte") connecting the omphaloid cavum with the discoplacental cavum. The latter is comparable with the deep mesometric groove in the gestation sac of the beaver.

The isolated position and high standing of the beaver amongst existing Rodents are primâ facie evidence of an exceedingly remote origin. Other facts of organisation and palæontology are in harmony with such evidence. These circumstances lend peculiar significance to the character of the preplacental blastocyst.

We may now give some attention to the behaviour of the inferior or obplacental hemisphere of the beaver's blastocyst. Without greatly enlarging the scope of the illustrations accompanying this paper, it would be impossible to do justice to the wonderful scenes of substitution of trophoblast for uterine epithelium, which can be witnessed in almost every section. In the preplacental blastocyst of the hedgehog, **Hubrecht** found a phagocytic trophoblast forming a complete trophosphere round the blastocyst. The ectoplacenta is a localised derivative of the trophoblast. **Resink**, however, applied the term "ectoplacenta" to the entire trophoblast. On the present occasion I propose to confine my remarks to Rodentia.

Obplacental ectodermal proliferations were described in the blastocyst of the rabbit by **A. von Kölliker** in 1882. According to **Kölliker** an event of fundamental importance for mammalian embryology was **Rauber's** discovery in 1875

of the so-called "Deckschicht" outside the formative epiblast of the rabbit's blastocyst, showing that the traditional view till then maintained by **Coste**, **Hensen**, and **Kölliker**, that the wall of the monodermic blastocyst had the value of embryonic ectoderm, was wrong. **Kölliker** called **Rauber's** "Deckschicht" the primitive ectoderm of the area embryonalis. Of next importance was **Lieberkühn's** demonstration in 1879 of the origin of the permanent or formative ectoderm of the rabbit out of the inner cell-mass which lies against the primitive ectoderm and splits into two layers—the permanent ectoderm and endoderm. **Kölliker's** primitive ectoderm of the rabbit's blastocyst thus prepared the way for **Hubrecht's** celebrated conception of the trophoblast of the mammalian blastocyst. In the extra-embryonic primitive ectoderm of the rabbit **Kölliker** discovered numerous ectodermal proliferations in the form of elongate, villiform elevations due to local nuclear divisions.

These papillæ were next described by **E. van Beneden** and **C. Julin** in 1884. On opening an eleven-day gestation sac of the rabbit under picrosulphuric acid, by a crucial incision through the antimesometric wall, a liquid escaped and a coagulum was produced. This was the fluid from the blastodermic cavity, which becomes the umbilical or vitelline vesicle or "yolk-sac." The cavity had been opened because the obplacental wall of the blastocyst was intimately united to the uterine mucosa. The union between the wall of the umbilical vesicle and the mucosa is effected by means of the epiblastic buds, which, as the authors stated, **Kölliker** first noticed. These buds arise upon the whole surface of the inferior hemisphere of the blastocyst, commencing about the eighth day. The degeneration of the cells, whose proliferation engenders the buds, begins at the ninth day, and leads to the rapid degeneration of the entire epiblastic membrane, which, at the fourteenth to fifteenth day, detaches in shreds from the mucosa.

M. Duval (1890, pl. iii, fig. 28) described and figured the bilaminar inferior hemisphere of the rabbit's blastocyst at the

tenth day, and observed the plasmodial swellings connected by intervening thin tracts, but he let them degenerate without having effected any useful purpose.

R. Assheton (1895) also mentioned and illustrated ('*Quart. Journ. Micr. Sci.*,' 37, Pl. 19, fig. 7) the obplacental papillæ of the rabbit. He says the first attachment of the blastocyst takes place between the lower parts of the blastodermic vesicle and the periplacental and obplacental folds of the uterus. It is effected by means of epiblastic papillæ about the eighth day. **Assheton** suggested that the papillæ became wedged into the uterine epithelium by reason of hydrostatic pressure from within the vesicle.

H. Schoenfeld (1902) made the first complete cytological study of the festoon-like adhesions of the preplacental blastocyst of the rabbit on the seventh and eighth days. At seven days the zona pellucida becomes broken on the antimesometric side of the blastocyst and multinucleated ectodermal thickenings have appeared. At 7 days 4 hours the ectodermal buds come into intimate adhesion with the uterine syncytium and push into it with pseudopodium-like processes so as to reach the maternal capillaries, thus fixing the blastocyst to the mucosa in a manner comparable to the rooting of a plant. From the seventh day of gestation until 8 days 4 hours, the blastocyst remains attached to the mucosa on the obplacental side. At 8 days 6 hours numerous plurimitotic figures occur in the epiblast of the obplacenta. At 8 days 22 hours **Minot's** giant-cells appear in the obplacental mucosa. They are of foetal origin, resulting from retrogressive changes of the obplacental multinucleated epiblastic buds, now embedded in the mucosa. At their origin they are much more voluminous than any elements belonging to the mucosa or submucosa. According to **Maximow**, they reach their maximum development, with a diameter of 100 μ , on the sixteenth to twentieth days.

J. Rejsek (1904) describes the obplacental implantation of the very young blastocyst of the Soudlik (*Spermophilus citellus*). It continues until the blastocyst acquires a

diameter of 2 mm., when it is given up simultaneously with the incipient placentation, which coincides in time with the cervical flexure of the embryo. The obplacental implantation is effected by means of a single multinucleate trophoblastic plasmodial proliferation at the antimesometric pole, sending processes into the mucosa. The number of nuclei increases by amitosis from 22 in a blastocyst of 0.126 mm. to more than 500. This obplacental implantation of the souslik's blastocyst would seem to be a phenomenon *sui generis*, the initial plasmodial thickening corresponding to a single papilla of the rabbit's blastocyst.

F. Muller (1905) also observed the antimesometric attachment of the preplacental blastocyst of *Sciurus* (vide his pl. viii. fig. 8).

For the characteristic features of the obplacental implantation of the preplacental blastocyst of the beaver, I must refer the reader to the foregoing text. The obplacental trophoblast is still connected with the uterine wall at the early placental stage, so that the implantation endures for a much longer period than in the rabbit. Eventually, when the invagination of the umbilical membrane is completed and the obplacental omphalopleure has vanished, giant-cells remain in the mucosa, appearing as white specks peppered over the internal surface of the gestation sac, scattered or in groups, not evenly distributed.

In the preplacental stage the trophoblast, at the areas of attachment, is not more than one layer in thickness and its cells remain distinct, though they may have several nuclei. It does not send processes to any depth into the mucosa, but as a rule it has a flat insertion upon the decidual surface, the maternal capillaries pressing towards the trophoblast rather than otherwise. Wherever the uterine epithelium is displaced by the obplacental trophoblast, it disappears without previously forming a syncytium. It is surprising to find the trophoblast planted like a pseudo-epithelium upon the decidual surface, and, at its borders, normal uterine epithelium. This probably means that the uterine epithelium becomes necrotic in

advance of the trophoblastic attack and that the trophoblast does not kill normal epithelium. When the mesometric glands degenerate, they do not form syncytia in the beaver, but the glandular epithelium becomes necrotic. The syncytia in the trophospongia at the early placental stage arise from a special proliferation of uterine epithelium, which takes place by mitosis in the mesometric region at the preplacental stage, before the ectoplacental proliferation of the trophoblast has set in.

XVI. BIBLIOGRAPHY.

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EXPLANATION OF PLATES 14 TO 21,

Illustrating Mr. Arthur Willey's paper on “The Blastocyst and Placenta of the Beaver.”

[Some of the drawings were reversed under the Edinger apparatus, and others were not reversed. It has not been thought necessary to